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BIOCHEMICAL BASES OF PATHOGENESIS OF HYPOKINESIA

Moscow KCSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 3-10

[Article by I. V. Fedorov, submitted 18 Sep 78]

[English abstract from source]

The paper describes an attempt to gain an insight into pathogenetic mechanisms and sequence of reactions responsible for changes in the metabolism of proteins, carbohydrates and fats of hypokinetic animals.

[Text] Hypokinesia has a dual effect on the body. There is decrease and change in flow of afferent and, consequently, efferent impulsation, and the body is deprived of their constant regulatory influence. The abrupt change from a state of movement and work to immobilization and rest acts as a stressor, and the greater the difference between these two states the stronger it is.

Direct and indirect evidence has been accumulated to date of the fact that there is decreased intensity of synthesis of tissular proteins and increased intensity of their breakdown in hypokinetic animals and man [1-6].

What are the mechanisms of change in protein metabolism of hypokinetic animals?

Protein synthesis is the unity of three flows: of energy, matter and information. Information about synthesis of individual proteins is contained in the appropriate structural genes, sections of the DNA molecule. According to our conceptions, blocking of the flow of information is the primary and decisive factor in lowering synthetic processes in the presence of hypokinesia.

According to total assays [7] by the method of Schmidt and Thannhauser in the modification of Tsanev and Markov, absolute DNA content of all tissues (with the exception of muscle) of hypokinetic animals did not change appreciably, whereas in muscle tissue it increased significantly.

We consider this to be a relative increase, occurring as a result of dissociation of myofibrillar and sarcoplasmic proteins, with preservation of nuclear material rich in DNA. As we see, no shortage of the substrate of information is demonstrable. RNA content of tissues, which was assayed by the same method, did not change or even increased. Most of the cellular RNA (over 80%) consists of ribosomal RNA (rRNA). But we are concerned mainly with messenger RNA (mRNA), the level of which did not exceed 2%. It is difficult to judge the changes in mRNA alone when assaying the sum of all cellular RNA.

The flow of information is limited primarily by the intensity of the transcription process. Afferent signals going to the central nervous system from functional muscles stimulate neural trophics, including the autonomic nervous system, which has an adaptive-trophic effect on all tissues, including skeletal muscles [8, 9]. It has been shown that an increase in gene activity, as manifested by increased activity of DNA-dependent RNA polymerase, i.e., intensity of the transcription process [10], is the basis of muscular adaptation to regular muscular exercise.

It is to be assumed that, in the presence of hypokinesia when there is significant attenuation and distortion [11] of afferent impulsation, there is a decrease in gene activity, since no derepression of structural genes occurs, which normally takes place under the influence of constant impulses from numerous interoceptors of functional muscles. Unfortunately, no determination was made of gene activity in hypokinetic animals. However, there are a number of facts serving as indirect proof of the validity of such hypotheses. Thus, giving immobilized animals a balanced (mainly protein) diet and anabolic hormones does not lead to restoration of protein synthesis in skeletal muscles. These processes start to recover only when the animals resume motor activity.

Hypokinesia, particularly during the first few weeks, acts like an unusual stress stimulus, which is confirmed by increased production of epinephrine, increased ACTH content of blood plasma [12-15], an increase in weight of the adrenals, hypertrophy of their cortex with proliferation of the fascicular layer, increased synthesis and secretion of corticosteroids [15-17]. The statistically reliable decrease in eosinophils of peripheral blood is also indicative of increased secretory activity of the adrenal cortex. At later stages of hypokinesia (over 60 days), there is development of depletion of the system of the hypothalamus-hypophysis-adrenal cortex, with corresponding decrease in adaptational capabilities of the organism.

Depression of synthetic and processes and activation of catabolic processes in most tissues is inherent in stress reactions, particularly in skeletal muscles, as was manifested in hypokinetic animals.

The influence on protein synthesis of changes in the other two flows (of matter and energy) is unquestionable, although it is not decisive.

Amino acids for protein synthesis arrive with feed proteins. During the first week of hypokinesia there is some decrease in feed intake; however, it then holds at the same level as in healthy animals [4, 18]. In the 2d-3d week of hypokinesia, total free amino acids in tissues, including muscle, increase by 10%, but there is a change in proportion of different amino acids [19].

With prolonged (60 days) hypokinesia, total amino acid content drops by almost 20%, mainly referable to unessential amino acids. This is related to increased excretion of amino acids in urine, use thereof to detoxify toxic products and as energy material. The shortage and imbalance of amino acids have an adverse effect on protein synthesis; however, most probably the change in information from structural genes is the primary cause of uneven utilization thereof in tissues: increased uptake of some and output of others. Then, the reaction apparently develops on the order of a vicious circle, as a result of which there is an even greater shortage and imbalance of some amino acids. The failure to normalize nitrogen equilibrium in hypokinetic humans by means of diet alone confirms our hypothesis. It is not such much a matter of shortage of material for protein synthesis as the impossibility of utilizing this material.

Potassium is one of the elements necessary for protein synthesis [20, 21]. On the 12th, 22d and 30th days of hypokinesia, the level thereof in rat muscles decreased by 12, 3 and 5%, respectively, of the control level [11, 22]. A substantial decrease is observed in potassium concentration in rabbit muslces 1 month after the start of hypokinesia [23]. In hypokinetic humans, there is increased excretion of potassium in urine.

The potassium deficiency can have an adverse effect on protein synthesis under hypokinetic conditions.

Protein synthesis requires energy. However, under hypokinetic conditions, metabolism of carbohydrates and lipids, oxidation of which produces most of the body's energy, is appreciably affected. The macroerg deficiency may be one of the causes of depression of synthetic processes.

Intensification of protein catabolism was manifested by increased excretion of products of their breakdown, negative nitrogen balance and decrease in absolute protein content of tissues.

As we see it, such a reaction is attributable to at least three causes. At the first stage (1st-3d weeks), hypokinesia acts like an unusual stress stimulus. The general response to any stressor is development of the catabolic phase of the general metabolic reaction. First of all, the process involves skeletal muscles, the products of breakdown of which are eliminated from the body and partially used as plastic material to maintain synthetic processes in vital organs. With increase in glucocorticoid production, there is stimulation of gluconeogenesis due to activation of tissue proteases and aminotransferases which are instrumental in protein breakdown [5, 24, 25].

It is known that when some part of the body is immobilized the components of its tissues are gradually destroyed. Thus, atrophy of extremital muscles is observed with the prolonged presence of a plaster cast, traumatic and surgical denervation, and tenotomy. This is so-called disuse atrophy. In the presence of hypokinesia, there is forced disuse of many muscle groups. It is not surprising then that proteins and other components of skeletal muscles begin to break down. This applies, first of all, to functionally active proteins, myofibrils and sarcoplasm. Cuthberson [26] made a study of sulfur and total nitrogen of urine in humans submitted to prolonged hypokinesia. He established that there is significant increase in elimination thereof, but the proportion between them remains the same as in proteins of skeletal muscles, which is indicative of predominant breakdown of the latter under hypokinetic conditions. One can also refer to partial destruction of skeletal muscles on the basis of tests on assimilation of creatine. It is known that creatine is assimilated by skeletal muscles. It was given with food. Before hypokinesia, over 80% of the creatine was assimilated and during hypokinesia assimilation decreased by 11-70%.

The third cause is as follows. The fact of the matter is that nitrogen, sulfur and phosphorus are excreted in urine in high quantities because considerably less of them can be utilized for synthetic processes.

In skeletal muscles, there is a decrease in share of myofibrillar and sarcoplasmic proteins and a corresponding increase in relative amounts of stromal proteins, proteins of fraction T [27, 28]. There is a significant increase in collagen content of skeletal muscles and the heart [29]. It should be assumed that these changes can have an adverse effect on functional capacity of muscles, particularly in the rehabilitation period following prolonged hypokinesia.

Carbohydrate metabolism undergoes a number of changes in hypokinetic animals. One of the typical ones is a decrease in glycogen content. Tissues became poor in the main substrate of respiration, glycogen [30, 33].

There was a change in blood sugar level concurrently with change in glycogen content.

Oxidation of carbohydrates was impaired. First, the aerobic route of their conversion was impaired. P/O coefficient decreased by 2-5 times, and there was dissociation of processes of respiration and phosphorylation [34-36]. Carbohydrate metabolism changed to energetically less advantageous anaerobic oxidation--glycolysis and glycogenolysis, and the intensity of the last two processes increased [33, 37]. At later stages (2-3 months) there was also depression of anaerobic processes [11, 33, 38].

As mentioned above, impairment of carbohydrate-energy metabolism affects protein synthesis and unquestionably has an adverse effect on conversion of other substances.

What are the causes of impairment of carbohydrate metabolism? Mobilization of carbohydrate resources by means of dissociation of glycogen in skeletal muscles and the liver is one of the usual manifestations of a stress reaction. Breakdown of glycogen is stimulated by increased access of epinephrine. Then, with increase in production of glucocorticoids, which activate the enzymes of gluconeogenesis and glycogen synthetase, there is a rise of glycogen level in the liver and skeletal muscles, as compared to the preceding stage (3d and 15th days), but it does not reach the base levels. There is depletion of protein and lipid resources as material for synthesis of glycogen. There is greater manifestation of glucogen requirement as energy material, since oxidative phosphorylation is depressed and there is prevalence of a less efficient route of macroerg production, glycogenolysis and glycolysis. The liver loses glycogen as a result of detoxification of breakdown products. Since there is accumulation of a large amount of products of protein breakdown in the presence of hypokinesia, detoxification thereof may be one of the causes of decrease in glycogen content of the liver.

Intensive dissociation of glycogen reserve and stimulation of gluconeogenesis cause hyperglycemia, which is inherent in the early stage of hypokinesia. At the later stages, hyperglycemia is replaced by persistent hypoglycemia, since by this time the store of glycogen is depleted, while de novo synthesis is inhibited. Increased sensitivity to insulin may also be involved in development of hypoglycemia [30].

According to I. A. Arshavskiy [39], motor activity is a factor in functional induction of anabolism. The data pertaining to change in glycogen content of skeletal muscles and the heart of hypokinetic animals confirm this. The myocardium functions continuously. By the 30th-60th day of hypokinesia, after initial stress dissociation, the glycogen reserve of the heart is restored almost to base levels due to de novo synthesis. By the 30th-60th days, there was still very little glycogen in skeletal muscles of the femur, which were virtually nonfunctional. The reserve thereof was not replenished under hypokinetic conditions. In the recovery period, however, after returning to the usual motor activity, glycogen content reached the base levels. There was a decline of glycogen level in the liver, as in muscles proper, with inactivity of skeletal muscles, and it was restored when they resumed activity. The main factor in impairment of carbohydrate-energy metabolism is the decreased production of macroergs due to dissociation of oxidation and phosphorylation in the respiratory chain. The intimate mechanisms of ATP production in oxidative phosphorylation have not yet been identified. For this reason, it is difficult to discuss the true causes of change in these processes under the influence of some factor or other, including hypokinesia. We conceive of the following sequence of reactions as a working hypothesis. Hypokinesia, acting like a stress factor, causes increased production of epinephrine [12-15]. Epinephrine activates lipases of fatty tissue and stimulates an increase in concentration of nonesterified fatty acids (NEFA) in tissues. Indeed, in hypokinetic rats

there is appreciable increase in lipase activity of fatty tissue and 1.5-2-fold increase in NEFA concentration. Free fatty acids are one of the factors of dissociation of oxidative phosphorylation [40] and increased mitochondrial permeability to other oxidation substrates. Both of these factors lead to a decline of P/O ratio. Moreover, utilization of NEFA as an oxidation substrate lowers P/O even more, since this involves elimination of one of the links of conjugation, due to formation of $NADP \cdot H_2$, rather than $NAD \cdot H_2$, at the first stage of β-oxidation.

In nonfunctioning muscles, there is no need to split ATP as a source of energy for muscular contraction. If there is no splitting of ATP there is no formation of ADP. The latter is a stimulator of oxygen uptake and formation of new ATP molecules in the course of oxidative phosphorylation.

With intensification of proteolysis, there is formation of superfluous ammonia, which binds oxalacetic and α-ketoglutaric acids, the main components of the tricarboxylic acid cycle (TCC). As a result, there can be a decrease in passage of reduced coenzymes from the TCC into the respiratory chain [41].

Energy of the respiratory chain is not used for ADP phosphorylation, but for active transport of substance and production of heat [38, 42].

With impairment of phosphorylation in the respiratory chain as the main supplier of macroergs, an emergency mechanism of energy supply is triggered, i.e., glycolysis [43]. In view of partial dissociation of respiration and phosphorylation, these processes can no longer successfully compete with glycolysis for ADP and phosphate. Expressly such a situation develops in the presence of hypokinesia. During the first weeks of hypokinesia, there is intensification of glycolysis and glycogenolysis in animals. There has been demonstration of stimulation of glycolysis in skeletal muscles of hypokinetic rats [44, 45]. This is also indicated by the numerous data pertaining to accumulation of lactic acid and some decrease in pyruvic acid in blood and tissues [6, 32, 33, 38]. Intensification of glycolytic processes compensates for the shortage of macroergs for only a brief time. Under hypokinetic conditions, there is considerable limitation of reserves of glycogen due to intensified breakdown and decreased synthesis thereof. Glycolysis and glycogenolysis become energetically less efficient, and for the production of the required amount of ATP considerably more substrates are used, which causes even greater depletion of the already sparse reserves. After 2-3 months, the shortage of carbohydrates and decreased activity of some glycogenolytic enzymes (phosphorylase, aldolase) [43-46] lead to weakening of the anaerobic route of carbohydrate conversion. Inhibition and blocking of glycolysis and the TCC under hypokinetic conditions induce compensatory increase in carbohydrate oxidation in the pentose cycle. Increased production of glucocorticoids, which is typical of hypokinesia, is also involved in intensifying direct oxidation of carbohydrates. However, the pentose cycle is chiefly a supplier of pentoses and $NADP \cdot H_2$, and to

a lesser extent macroergs. They become more intensively involved in lipid metabolism to compensate for the shortage thereof.

A number of changes in lipid metabolism was demonstrated in hypokinetic rats and rabbits [6, 29, 47-49]. In animals (particularly rats) there was a decrease in lipid reserves and substantial decrease in total lipids of tissues. There was an increase in cholesterol content of blood and tissues of rat skeletal muscles, heart, liver and kidneys. Studies of blood serum lipoproteins of hypokinetic rats by the method of disk electrophoresis on polyacrylamide gel showed an increase in the pre-β-lipoprotein fraction, β-lipoproteins, as well as albumins in a complex with NEFA. The increase in levels of these fractions indicated that, under hypokinetic conditions, there was an increase in endogenous triglycerides (pre-β-lipoproteins), cholesterol (β-lipoproteins) and NEFA in the animals' blood. In rats, there was a 30-45% increase in lipolytic activity of fatty tissue. There was concurrent increase in serum NEFA content, from 50 to 129%. There was a drastic increase in acetone body content (to 470%).

There is much in common between the genesis of disturbances referable to carbohydrate and lipid metabolism under hypokinetic conditions, in view of the close correlation between conversions thereof in the body. Stress caused by hypokinesia induces an increase in production of epinephrine and glucocorticoids. Both hormones are involved in mobilizing lipids from the fat depot. In the presence of hypokinesia, there is substantial increase in fatty tissue lipase activity under the influence of epinephrine and glucocorticoids, which leads to an increase in NEFA content. Intensification of lipolytic activity is one of the causes of depletion of fat depots and decrease in lipids of skeletal muscles and liver, as well as decline of triglyceride levels in many tissues after 15 and 30 days of hypokinesia. Impairment of carbohydrate metabolism is the second cause. As we know, the blood glucose level regulates lipid synthesis and breakdown. In rats, one observes hypoglycemia, decreased intensity of carbohydrate metabolism via the glycolytic and, particularly, oxidative pathways. When there is a glucose deficiency, there is increased breakdown of lipids and inhibition of de novo production thereof. Glycerophosphate is needed for lipogenesis, and it is generated in the course of glycolysis. Under normal conditions, NEFA are metabolized very rapidly, so that the levels thereof are low in serum. Under hypokinetic conditions, conversion of NEFA is slower. This is attributable to several causes. There is faster breakdown of triglycerides than utilization thereof, in particular due to the fact that liposynthesis is inhibited by the shortage of glucose, and there is not enough glycerophosphate. Citrate activates one of the main enzymes of fatty acid synthesis, acetyl-CoA-carboxylase, and there is less access of citrate when the TCC is blocked.

The subsequent fate of fatty acids is oxidation in the β-cycle, with formation of acetyl-CoA. In hypokinetic animals, the reserves of free acetyl-CoA are replenished by means of intensified breakdown of carbohydrates and conversion of glucogenic amino acids, in addition to β-

oxidation. An overt surplus of this important substrate is formed. In healthy animals, active acetic acid, which burns up in the TCC, delivering hydrogen to the oxidative chain, is used for synthesis of cholesterol, fatty acids and acetone bodies. As shown above, under hypokinetic conditions there is impairment of oxidation of acetyl-CoA in the TCC, with dissociation of processes of oxidation and phosphorylation in the respiratory chain and inhibition of de novo synthesis of fatty acids. In this situation, synthesis of cholesterol and acetone bodies are the chief means of utilizing active acetic acid. Indeed, a substantial increase in blood and tissue cholesterol content and blood β-lipoprotein content, the main transport form of cholesterol, was observed in hypokinetic animals. The levels were particularly high on the 15th and 90th days of hypokinesia. At expressly these times there was demonstration of maximum increase in enzymes of the pentose cyde--glucose-6-phosphate dehydrogenase and 6-phosphogluconic acid dehydrogenase, which delivers the $NADP \cdot H_2$ product required for cholesterol synthesis. Along with increase in cholesterol content, there was a significant increase in acetone bodies; consequently, part of the accumulated surplus of acetyl-CoA was used to produce them. The carbohydrate deficiency was also involved in this. The cholesterol surplus depresses glycolysis [50] which, in turn, is instrumental in impairment of fat metabolism, with respect to even more production of cholesterol and acetone bodies. The vicious circle closes. Such parameters of carbohydrate and fat metabolism as depletion of glycogen reserve, emptying of fat depots, lipemia and acetonemia are observed in the presence of hypokinesia and diabetes mellitus. It is quite likely that a shortage of insulin is one of the causes of this, as is the case with diabetes. There are no data in the literature concerning insulin levels in hypokinetic animals and man. However, there are grounds to assume that insulin content was relatively low, since there was a substantial increase in production of its antagonists, epinephrine, glucocorticoids and adrenocorticotropic hormones.

These are, in our opinion, the causes of changes in fat metabolism of animals submitted to rigid hypokinetic conditions.

In the presence of hypokinesia, there is a change in composition of many tissues, particularly skeletal muscles, in the direction of sclerosis, replacement of part of the active proteins of sarcoplasm and the actomyosin complex with connective tissue proteins. A quantitative evaluation of these processes was first made by P. P. Potapov [29], who assayed collagen (according to hydroxyproline), total (according to glucosamines) and acid (according to hexuronic acids) mucopolysaccharides.

Collagen content of skeletal muscles increased by 40% on the 15th day of hypokinesia and by 48% on the 60th-90th days, as compared to the control. Hexosamine content decreased by 8.6, 9.4 and 19.6% on the 15th, 30th and 90th days, respectively, while hexuronic acid content reliably increased. By the 60th-90th days, hydroxyproline content also increased in the myocardium and kidneys, and did not change in the liver. At all tested

times, there was an appreciable decrease in hexosamine content of the liver, and by the 90th day there was also one in the kidneys. At all times, hexuronic acid content was high in the kidneys, it declined somewhat in the heart and did not change in the liver.

Thus, under hypokinetic conditions there is a significant change in mucopolysaccharide content of many tissues. Fluctuations thereof could play a substantial role in development of disturbances referable to fluid-base equilibrium and tissular permeability; they could be involved in decreasing resistance to infection and affect clotting of blood. As we have already noted, under hypokinetic conditions there is less intensive oxidative phosphorylation, compensatory increase in glycolysis and direct oxidation of glucose. The change to less efficient means of utilizing carbohydrates results in a decrease in resources thereof in the organism. Phosphoric esters of hexoses are the direct precursors of hexosamines and hexuronic acids. One of the chief causes of change in their levels under hypokinetic conditions is a shortage of carbohydrates. The other causes are related to changes in glucocorticoid production and cholesterol content. As we know, adrenocortical hormones depress synthesis of glycosaminoglycans, while cholesterol stimulates production of acid mucopolysaccharides. The increase in connective tissue elements of skeletal muscles can lead to impairment of their function, particularly during the period of readaptation following prolonged hypokinesia. It is possible to make a quantitative evaluation of development of sclerotic processes in skeletal muscles and the heart according to collagen content. A significant increase in the latter, especially at the late stages of hypokinesia, is attributable to an increase in amount of acid mucopolysaccharides, which induce collagen synthesis. On the 60th and 90th days, there is a 42 and 38% increase, respectively in hydroxyproline/hexuronic acid ratio in intramuscular connective tissue. The same direction of changes is inherent in the heart. This is indicative of a shortage of the main substance of connective tissue and its aging.

BIBLIOGRAPHY

1. Fedorov, I. V.; Vinogradov, V. N.; Milov, Yu. I.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1967, pp 53-57.

2. Fedorov, I. V.; Milov, Yu. I.; and Simonov, Ye. Ye. Ibid, No 3, 1970, pp 18-21.

3. Fedorov, I. V.; Chernyy, A. V.; and Fedorov, A. I. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 8, 1977, pp 1128-1133.

4. Fedorov, I. V., and Grishanina, L. A. KOSMICHESKAYA BIOL., No 3, 1967, pp 43-48.

5. Fedorov, V. I. Ibid, No 5, 1971, pp 82-84.

6. Fedorov, I. V. NAUCH. DOKL. VYSSH. SHKOLY. BIOL. NAUKI [Scientific Reports of Schools of Higher Education. Biological Sciences], No 12, 1972, pp 24-36.

7. Fedorov, I. V., and Shurova, I. F. KOSMICHESKAYA BIOL., No 2, 1973, pp 17-21.

8. Orbeli, L. A. "Selected Works," Moscow-Leningrad, Vol 2, 1962, pp 94, 227, 413, 427.

9. Yakovlev, N. N. "Biochemistry of Sports," Moscow, 1973, pp 53-67, 77-88, 129-136, 205-212.

10. Rogozkin, V. A.; Zil'ber, M. L.; and Pliskin, A. V. VOPR. MED. KHIMII [Problems of Medical Chemistry], No 4, 1974, pp 376-379.

11. Zhukov, Ye. K.; Barbasheva, Z. I.; and Fedorov, V. V. FIZIOL. ZH. SSSR, No 9, 1971, pp 1240-1245.

12. Krupina, T. N.; Mikhaylovskiy, G. P.; and Tizul, A. Ya. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii" [Adaptation to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 94-96.

13. Krupina, T. N.; Tizul, A. Ya.; Baranova, V. P.; et al. Ibid, pp 96-98.

14. Kazaryan, V. A.; Pishchik, V. B.; and Shipov, G. D. Ibid, pp 79-80.

15. Kovalenko, Ye. A.; Mailyan, E. S.; Popkov, V. L.; et al. USPEKHI FIZIOL. NAUK [Advances in Physiological Sciences], Vol 6, 1975, p 3.

16. Kovalenko, Ye. A. KOSMICHESKAYA BIOL., No 1, 1976, pp 3-15.

17. Parin, V. V.; Fedorov, B. M.; and Nevstruyeva, V. S. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 184, No 1, 1969, pp 250-251.

18. Kovalenko, Ye. A.; Popkov, V. L.; Kondrat'yev, Yu. I.; et al. PAT. FIZIOL. [Pathological Physiology], No 6, 1970, pp 3-8.

19. Fedorov, I. V. KOSMICHESKAYA BIOL., No 5, 1973, pp 35-39.

20. Kovtunyak, N. A., and Meshchishen, I. F. NAUCH. DOKL. VYSSH. SHKOLY. BIOL. NAUKI, No 8, 1971, pp 38-44.

21. Mirskiy, N. P., and Osava, S. in "Funktsional'naya morfologiya kletki" [Functional Morphology of the Cell], Moscow, 1963, pp 9-68.

22. Mikhaleva, N. P.; Ivanov, I. I.; Korovkin, B. F.; et al. in "Eksperimenty issledovaniya gipokinezii, izmenennoy gazovoy sredy, uskoreniy, peregruzok i drugikh faktorov" [Experimental Studies of Hypokinesia, Altered Gas Environment, Accelerations, G Forces and Other Factors], Moscow, 1968, pp 18-21.

23. Krotov, V. P. KOSMICHESKAYA BIOL., No 2, 1972, pp 66-74.

24. Fedorov, I. V.; Milov, Yu. I.; Vinogradov, V. N.; et al. Ibid, No 1, 1968, pp 22-24.

25. Simonov, Ye. Ye., and Fedorov, I. V. Ibid, No 1, 1970, pp 16-18.

26. Cuthberson, D. P. BIOCHEM. J., Vol 23, 1929, pp 1328-1345.

27. Mikhaleva, N. P.; Ivanov, I. I.; Fedorov, I. V.; et al. KOSMICHESKAYA BIOL., No 2, 1970, pp 42-45.

28. Gayevskaya, M. S.; Slez, L. M.; and Ilyushko, N. A. Ibid, No 4, pp 25-29.

29. Potapov, P. O. "Glycosaminoglycans (Mucopolysaccharides), Collagen and Lipids of Tissues in the Presence of Hypodynamia," author abstract of candidatorial dissertation, Moscow, 1978.

30. Chernyy, A. V. KOSMICHESKAYA BIOL., No 1, 1975, pp 23-27.

31. Vinogradov, V. N.; Petrukhin, V. G.; and Fedorov, I. V. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 6, 1968, pp 96-99.

32. Blinder, L. V.; Organov, V. S.; and Potapov, A. N. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii," Novosibirsk, 1970, pp 37-37.

33. Rassolova, N. P.; Potapova, A. N.; Sapelkina, I. M.; et al. KOSMICHESKAYA BIOL., No 2, 1973, pp 26-33.

34. Ivanova, S. M., and Ushakov, A. S. in "Fiziologicheskiye problemy detrenirovannosti" [Physiological Problems of Deconditioning], Moscow, 1970, pp 118-121.

35. Kovalenko, Ye. A.; Popkov, V. L.; Mailyan, E. S.; et al. KOSMICHESKAYA BIOL., No 4, 1971, pp 3-8.

36. Mailyan, E. S.; Brinberg, L. N.; and Kovalenko, Ye. A. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii," Novosibirsk, 1970, pp 11-112.

37. Siryk, L. A. BYULL. EKSPER. BIOL., No 10, 1972, pp 22-25.

38. Siryk, L. A., and Tregulov, M. I. Ibid, No 10, 1973, pp 21-24.

39. Arshavskiy, I. A. in "Vedushchiye faktory ontogeneza" [Prime Ontogenetic Factors], Kiev, 1972, p 44.

40. Skulachev, V. P. "Accumulation of Energy in Cells," Moscow, 1969.

41. Gulyy, M. F. "The Main Metabolic Cycles," Kiev, 1968, pp 207-226.

42. Grinberg, L. N. in "Mitokhondrii. Struktura i funktsii v norme i patologii" [Mitochondria: Structure and Functions Under Normal and Pathological Conditions], Moscow, 1971, pp 145-150.

43. Ivanov, I. I.; Korovkin, B. F.; and Mikhaleva, N. P. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 99-107.

44. Barbashova, Z. I.; Zhukov, Ye. K.; Baklanova, S. M.; et al. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii," Novosibirsk, 1970, pp 26-35.

45. Ryl'nikov, Yu. P., and Fedorov, I. V. in "Povolzhskaya konf. fiziologov s uchastiyem biokhimikov, farmakologov i morfologov. 6-ya. Materialy" [Proceedings of 6th Povolzh'ye Conference of Physiologists, With the Participation of Biochemists, Pharmacologists and Morphologists], Cheboksary, Vol 2, 1973, p 126.

46. Starostin, V. I.; Portugalov, V. V.; and Il'ina-Kakuyeva, Ye. I. DOKL. AN SSSR, Vol 190, No 5, 1970, pp 1215-1217.

47. Lobova, T. M. KOSMICHESKAYA BIOL., No 5, 1973, pp 32-35.

48. Fedorov, I. V.; Ryl'nikov, Yu. P.; and Lobova, T. M. KARDIOLOGIYA [Cardiology], No7, 1973, pp 50-54.

49. Ryl'nikov, Yu. P. KOSMICHESKAYA BIOL., No 2, 1974, pp 8-13.

50. Sidorenkov, I. V., and Gil'miyarova, F. N. VOPR. MED. KHIMII, No 3, 1969, pp 250-253.

EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 612.13/.15-06:629.78

RESULTS OF STUDIES OF PULSED BLOOD FLOW AND REGIONAL VASCULAR TONUS DURING FLIGHTS IN THE FIRST AND SECOND EXPEDITIONS ABOARD THE SALYUT-6--SOYUZ ORBITAL COMPLEX

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 11-14

[Article by V. F. Turchaninova and M. V. Domracheva, submitted 10 May 79]

[English abstract from source]

The dynamics of pulse blood filling and regional vascular tone was studied in the crewmembers of 96- and 140-day flights aboard the station Salyut-6—Soyuz. Measurements were taken before, during and after flights, using a specially designed tetrapolar rheograph. Rheograms of the torso, forearms, legs, and rheoencephalograms of the right and left hemispheres in the frontal-mastoidal lead were recorded. The results showed that in zero-g the cosmonauts developed typical hemodynamic changes indicative of cephalad blood shifts. Thus, the hypothesis advanced and theoretically substantiated previously has found further support.

[Text] The conception has been formed at the present time that there is redistribution of fluids, particularly blood, in a cranial direction in the human body in weightlessness. This hypothesis was based primarily on the sensations of a rush of blood to the head, which cosmonauts experience, as well as theoretical analysis of the influence of weightlessness on human functional systems. In addition, some objective data were obtained during flights: shifting of the center of mass toward the head, demonstrated by photography of facial puffiness in infrared light, dilatation of veins in the upper part of the body, reduction in diameter of the lower limbs and in size of the legs and thighs on the 3d flight day [1]. Arteriovenous pulsography demonstrated increased filling and pressure of jugular veins [2, 3].

Our objective here was to study the dynamics of pulsed blood flow [filling] and regional tonus of different parts of the body in the course of 96- and 140-day flights.

Methods

Rheograms of the trunk, arm and leg, at rest, were taken with a specially developed tetrapolar rheograph before, during and after space flights, as well as rheoencephalograms. The onboard rheograph records not only the rheographic curve, but a calibration signal that is proportionate to the value of the constant component of impedance. In accordance with this arrangement of the instrument, determination of the index of pulsed filling (PF = $\Delta R/R$) is made by finding the ratio of rheogram amplitude to the calibration signal ($\Delta R/R = A/K \cdot const$); the value of the constant depends on the region examined, and it is given in the technical specifications of the instrument. Another distinction of this instrument is that the required amplification and range of measurement of R/R is made by altering the position of the switch for modes of instrument operation.

Background studies were made at different stages of the preflight period. During the flights, the rheogram of the trunk and rheoencephalogram were recorded at approximately the same intervals throughout the period of weightlessness. Rheograms of the extremities were recorded on the 14th and 24th days for the crew of the first expedition; on the 21st, 68th, and 110th days for the commander in the second expedition, 4th, 63d and 119th days for the flight engineer in the second expedition.

When interpreting the rheograms, in addition to the pulsed and minute flow indices, we calculated the conventional indices of tonus of vessels of different caliber. In addition, we determined cardiac stroke volume (SV) and minute volume of circulation (MV) using the formula of A. A. Kedrov [4, 5].

Results and Discussion

SV increased in 3 out of 4 cosmonauts on the 4th-7th flight days. Thereafter, there were usually insignificant fluctuations, and more significant deviations were only observed in a few cases: SV increased by 25% on the 82d day in the commander of the first expedition; it decreased by 25% on the 63d day in the commander and on by 28% on the 119th day in the flight engineer of the second expedition. At the same time, SV was essentially somewhat low throughout the flight of the flight engineer of the first expedition (by 2-15%). In virtually all of the cosmonauts, MV exceeded the mean preflight level or did not differ from it. After the flights, there was prevalence of low SV and MV in the crew of the first expedition as well: the levels were not restored for 11 days.

Figures 1 and 2 illustrate the dynamics of filling of vessels of the head, showing that pulsed and minute filling of cerebral vessels as increased in both cosmonauts (more so in the flight engineer) during the 96-day mission, and did not diminish by the end of the flight. During the 140-day mission, we also observed an appreciable increase in filling of

cerebral vessels which, however, did not differ from the preflight level or even diminished during the second half of the mission. The interhemispheric asymmetry of filling observed about half way through the flight decreased or disappeared entirely by the end of the mission. Filling remained increased in the crew of the first expedition on the 3d postflight day, and it did not present positive dynamics in the flight engineer. Filling with blood increased by 55-65% in the commander and decreased by 55-67% in the flight engineer on the 9th day after the 140-day mission.

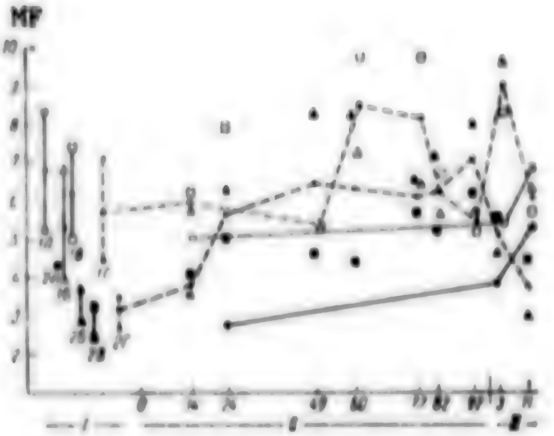

Figure 1.
Dynamics of filling of vessels of the brain and leg in the commander (1) and flight engineer (2) of the first main expedition
Here and in Figure 2:
A) index of filling of leg vessels
Б) index of filling of right hemisphere vessels
B) index of filling of left hemisphere vessles
Г) mean filling index for vessels of right and left hemispheres
I) before flight
II) during flight
III) after flight
MF) index of minute filling with blood

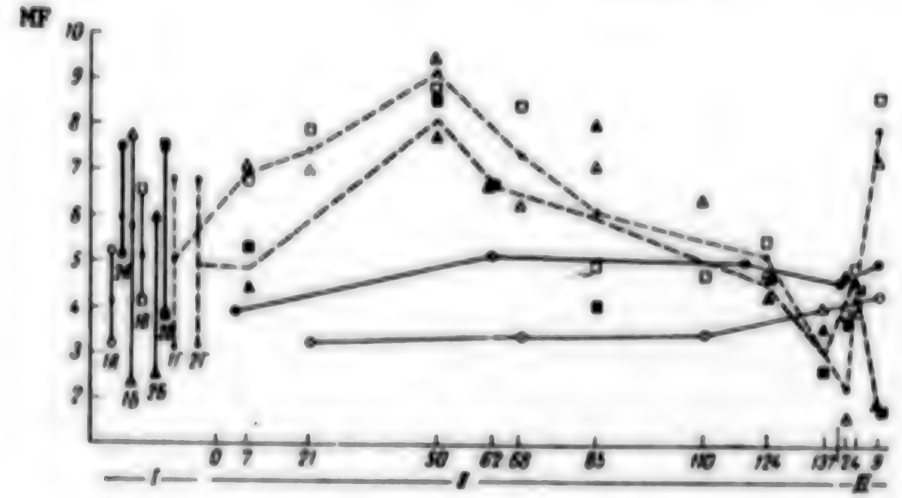

Figure 2. Dynamics of indices of vascular filling in the brain and leg of commander (1) and flight engineer (2) in second main expedition

There was less filling with blood of leg vessels during the flight and on the 2d-3d postflight day than before it. There was a mild tendency toward normalization thereof in the second half of the flight of cosmonauts participating in the second expedition (see Figures 1 and 2). At the same time, flow to the forearm exceeded the preflight level or did not differ from it, whereas on the 2d-3d postflight day it usually diminished somewhat.

In three out of four cosmonauts, arteriolar and venous tonus of cerebral vessels essentially diminished during the flights, and in some cases quite significantly, which was manifested by a change in form of the rheoencephalograms (the notch shifted below the isoelectric line). At the same time, there was no consistent pattern to changes in tonus of small vessels in the flight engineer of the second expedition, and its indices were within the range of preflight levels. After the mission, arteriolar tonus usually remained diminished, and it increased in only one cosmonaut. In addition, venous tonus decreased only in the crew of the first expedition, and it did not recover on the 11th day. The changes in arteriolar and venous tonus of the forearm and leg of different cosmonauts were individual in nature; however, in most cases there was a pattern, as manifested by opposite dynamics of tonus of small vessels of the forearm and leg. After the flight, tonus of arterioles and veins of the forearm diminished in three cosmonauts, whereas in the flight engineer of the second expedition it increased, with concurrent increase of tonus in the legs of all crew members.

Thus, according to the rheographic findings, there was expression of the following changes in central and regional hemodynamics: initial (4th-7th days) increase in SV in 3 out of 4 cosmonauts; a tendency for MV to exceed preflight levels throughout the flight and decrease in volume of circulation after the flight; increased pulsed and minute filling of cerebral vessels, which reverted to preflight levels after 85-110 days of the 14-day mission; both parameters remained high after the 96-day flight and diminished after the 140-day flight; appearance of marked asymmetry of filling of cerebral vessels on the 49th-77th day in the first crew and on the 85th flight day in the second crew, with equalization by the end of the flight; decreased filling of leg vessels during and after flight, with concurrent increase or absence of change in filling of forearm vessels (only during flight); diminished arteriolar and venous tonus of cerebral vessels of three cosmonauts during and after flight; changes in different directions in arteriolar and venous tonus in the forearm and leg, the deviations being individual in nature in different crew members.

The changes in central and regional hemodynamics during the space flights may be attributable to several factors, the chief ones being redistribution of blood and functional loads on vessels of different parts of the body, development of deconditioning of muscles and decreased role thereof as

a venous pump. According to current conceptions [6, 7], in weightlessness blood and tissular fluid shift in a cranial direction, and this probably leads to the initial increase in SV and MV demonstrated in our studies. Perhaps, this is also related to the increase in pulsed flow to cerebral vessels with concurrent decrease in pulsed flow to the leg. In view of the fact that the rheographic studies were made starting only on the 4th-7th days, the decrease in arteriolar and venous tonus of cerebral vessels may be interpreted as the result of an adaptive reaction helping to imporve efflux of blood and preventing development of venous stasis. Dilatation of the atria and central veins due to the hemodynamic changes at the early stage of weightlessness apparently leads to subsequent decrease in circulating blood volume, which has been found in a number of postflight studies [8]. We cannot rule out the possibility that this is the cause of normalization of SV, which developed by the end of the 2d-3d weeks of the flights.

A comparison of our results to those of model studies (antiorthostatic [head down] hypokinesia for 49 days) revealed that the reaction referable to SV during the flights and with exposure to factors simulating weightlessness was in approximately the same direction and of the same duration. As for increased filling of cerebral vessels, the increment was more marked during the flight and normalization occurred only on the 85th-110th days. All this warrants the conclusion that the redistribution of blood in a cranial direction in weightlessness is more persistent and associated with greater increase in pulsed filling of cerebral vessels, against the background of significant decline of indices of arteriolar and venous tonus, than observed under antiorthostatic hypokinetic conditions with a -4° tilt.

The causes of the observed asymmetry in filling of vessels of the right and left hemispheres in some of the in-flight studies are not quite clear. We can only assume that the observed asymmetry reflects individual distinctions of anatomical structure, vascular tonus and reactivity, which become more marked or are manifested only when there is considerable increase in filling. Moreover, the opinion is held that asymmetry of filling of cerebral vessels may be indicative of development of vegetovascular dysfunction, i.e., more or less marked changes in function of vasomotor centers [9]. However, this hypothesis requires verification.

Thus, the existing hypothesis of redistribution of blood in the human body under the influence of weightlessness has obtained additional confirmation.

BIBLIOGRAPHY

1. Thornton, W. E.; Hoffler, G. W.; and Rummel, J. A. in "Skylab Life Sciences Symposium Proceedings," Houston, Vol 11, 1974, pp 211-232.

2. Yuganov, Ye. M.; Degtyarev, V. A.; Nekhayev, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1977, pp 31-37.

3. Degtyarev, V. A.; Nekhayev, A. S.; Bednenko, V. S.; et al. Ibid, No 4, 1979, pp 8-12.

4. Kedrov, A. A. KLIN. MED. [Clinical Medicine], No 1, 1941, pp 71-76.

5. Idem, Ibid, No 5, 1948, pp 266-271.

6. Gazenko, O. G.; Gurovskiy, N. N.; Bryanov, I. I.; et al. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy" [Summaries of Papers Delivered at 10th Symposium on Space Biology and Medicine], Moscow, 1977, pp 13-14.

7. Kovalenko, Ye. A. in "Nevesomost'" [Weightlessness], Moscow, 1974, p 243.

8. Johnson, R. L. in "Man in Space," Moscow, 1974, pp 142-159.

9. Yarullin, Kh. Kh., and Vasil'yeva, T. D. KOSMICHESKAYA BIOL., No 3, 1977, pp 20-26.

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CIRCULATION IN EXERCISING CREW MEMBERS OF THE FIRST MAIN EXPEDITION ABOARD SALYUT-6

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 15-18

[Article by V. S. Georgiyevskiy, N. A. Lapshina, L. Ya. Andriyako, L. V. Umnova, V. G. Doroshev, I. V. Alferova, V. N. Ragozin and Ye. A. Kobzev, submitted 26 Dec 78]

[English abstract from source]

During the 96-day flight aboard the Salyut-6 station the crewmembers showed a satisfactory response to bicycle ergometry of moderate load. However, cardiovascular regulation during exercise declined, particularly by the end of the first and the beginning of the second month. This was mainly associated with deconditioning due to an inadequate work load. Its increase helped to restore an initial level of circulation during exercise by the end of the mission.

[Text] Since the first missions, exercise was used extensively in clinical and physiological studies of cosmonauts, and later aboard the Salyut and Skylab orbital stations [1-5]. This article deals with a study of the changes in the cardiovascular system during exercise in the course of a 96-day orbital flight.

Methods

An onboard bicycle ergometer was used for the physical load test. The subjects had to perform exercise constituting 3750 kg-m within 5 min of pedaling at a mean rate of 750 kgm/min and speed of 60 r/min. It actually fluctuated on different test days from 3010 to 4050 kg-m in the commander and flight engineer, i.e., it was on the level of average load.

Polynome-2M equipment was used to record the tachooscillogram, kinetocardiogram from the region of the apex beat and sphygmogram of the femoral artery [6]. Mean dynamic, lateral systolic, end systolic and pulse arterial pressure (AP) were determined from the tachooscillogram. The

kinetocardiogram served to find isovolumetric contraction (IC) and period of ejection (PE) for the left ventricle. We measured the pulse wave velocity (PWV) over the descending aorta. We calculated stroke (SV) and minute (MV) volumes of circuation, specific real resistance (SAR), ejection of minute blood volume (EMBV), interphase (IF) and intrasystolic (IS) indices. The parameters were recorded before and within 2-3 min after pedaling. In addition, there was continuous monitoring of heart rate (HR) and recording of the EKG in the DS lead.

Results and Discussion

Both cosmonauts tolerated the exercise tests satisfactorily throughout the flight aboard the orbital station: they felt well; they did not experience pain or other unpleasant sensations. However, immediately after they stopped pedaling, the cosmonauts had the feeling of blood rushing to the head, and there were signs of intensive regulation of circulation.

The most marked cardiovascular reactions were demonstrated in both cosmonauts on the 24th flight day. In spite of the fact that pedaling time was reduced to 3 min 18 s for the commander and to 4 min 30 s for the flight engineer, maximum HR increased to 144 and 145/min, respectively (before the flight, this parameter constituted 138 and 114/min). A "stable state" was not reached with respect to pulse rate. In the flight engineer, lateral systolic and particularly end systolic AP were above preflight levels. There was also relative increase in IC, decrease in PE, increase in IF and decrease in IS (see Table).

It should be noted that the first signs of change in regulation of circulation were demonstrable already on the 7th flight day, although the test was well-tolerated at that time. As a result of the physical load, there was an increase by more than 4 m/s in PWV, although it had also been somewhat higher than the preflight level before the test. AP dropped as a result of exercise in the commander. In addition, we observed stepped change in end systolic AP (in the 2d min after the load it was lower than in the 3d), which is usually related to overfatigue or stress [7]. The nature of the AP reaction did not change in the flight engineer.

Of special interest are the dynamics of duration of the PE period. As a result of the exercise, it became shorter in the commander, both as compared to the level on the ground and appropriate level. We had observed significant shorting of the PE and relative extension of IC after exercise in our previous studies [2, 3], and we interpreted this as a signed of decreased venous return. The decrease in IS and EMBV was indicative of the same thing.

According to the general hemodynamic indices, we could assume that endurance of the test by the commander improved on the 42d day. In spite of the increase in amount of exercise to 4050 kg-m, maximum HR during

exercise, AP and PWV after it corresponded to preflight levels. However, there were changes in intracardiac hemodynamics indicative of decreased venous return.

Circulatory parameters during test on bicycle ergometer

Period	Time after pedaling, min	HR/min	AP, mm Hg: minimum	AP, mm Hg: mean dynamic	AP, mm Hg: lateral systolic	AP, mm Hg: end systolic	IC, s	PE, s	PWV, m/min	SV, ml	MV, L/min
Commander											
Before flight	BG	64	71	98	121	150	0,050	0,284	6,0	123	7,8
	1	75	79	104	135	166	0,035	0,230	8,0	80	6,0
	2	70	80	96	122	154	0,030	0,250	9,1	57	4,0
Weightlessness, days: 7th	BG	68	78	113	132	153	0,060	0,262	10,0	69	4,4
	1	96	—	—	—	—	0,030	0,185	—	—	—
	2	67	74	103	124	144	0,030	0,235	14,6	36	2,4
24th	BG	58	68	100	115	153	0,060	0,300	4,9	145	8,5
	1	90	70	109	140	172	0,035	0,185	7,7	83	7,5
	2	74	68	98	128	155	—	0,250	8,1	126	9,3
42d	BG	68	63	89	108	140	0,054	0,287	6,1	111	7,6
	1	111	81	107	125	175	0,042	0,225	8,9	68	7,6
	2	78	74	98	175	158	0,040	0,255	8,1	85	6,6
70th	BG	72	69	96	115	150	0,055	0,245	7,0	81	5,8
	1	114	78	109	125	180	0,038	0,224	—	—	—
82d	BG	64	66	102	112	150	0,040	0,280	5,8	113	7,3
	1	86	65	111	127	175	0,037	0,220	9,1	78	6,7
	2	77	80	118	130	160	—	—	—	—	—
Flight engineer											
Before flight	BG	51	63	90	116	143	0,055	0,316	7,4	118	6,0
	1	70	74	93	136	167	—	—	—	—	—
	2	67	70	94	130	176	0,030	0,270	8,4	102	6,8
Weightlessness, days: 7th	BG	60	66	84	108	139	0,057	0,280	8,15	75	4,5
	1	90	60	89	114	162	0,030	0,170	11,7	64	5,8
	2	74	58	87	112	147	—	0,240	12,5	64	4,0
24th	BG	56	58	78	98	128	0,051	0,300	5,8	119	6,6
	1	120	68	100	135	180	0,037	0,180	11,6	60	7,2
	2	97	70	97	122	180	—	0,194	11,9	46	4,4
42d	BG	64	62	83	99	138	0,053	0,300	6,8	91	5,8
	1	88	65	87	111	168	0,039	0,230	9,4	63	5,5
	2	78	63	84	105	152	—	0,254	10,0	60	4,7
70th	BG	67	66	88	104	142	0,056	0,284	5,8	110	7,3
	1	105	68	100	122	180	0,045	0,180	10,0	53	5,5
	2	98	66	90	112	178	0,047	0,225	8,5	71	7,0
82d	BG	64	60	82	97	130	0,049	0,289	5,9	95	6,0
	1	114	70	95	124	174	0,035	0,228	9,7	84	9,6
	2	96	72	95	122	175	0,035	0,237	8,8	80	7,6

Key: BG) background

On the 42d flight day, the flight engineer performed less exercise (2495 kg-m). His circulatory reaction was poorer than before the flight; as a result of exercise HR increased, while PE decreased.

There was substantial improvement of the commander's endurance of the test on the 70th and 82d flight days, as compared to the preceding tests. The main circulatory parameters were close to preflight levels. However, there were some elements inherent in unstable reactions. With lower values for lateral systolic, dynamic mean and minimum AP, there was a high end systolic level and relatively higher PWV.

On the 70th day, the flight engineer increased the pedaling rate to the specified level and maintained it rather well for the entire 5 min; however, his circulatory reaction was somewhat poorer than before the flight. By the 82d day, he presented significant improvement of circulatory regulation during exercise. Circulatory parameters came close to preflight levels, although we did observe a somewhat higher HR, end systolic AP, PWV and somewhat lower SV, IC and PE.

Special mention should be made of the fact that, at this time, there was restoration in both cosmonauts of the preflight correlation between duration of IC and PE, i.e., the syndrome of myocardial hypodynamia disappeared.

It may be assumed that deconditioning was the chief cause of poorer endurance of the exercise test. As we have already noted, the first signs thereof were noted in the commander on the 7th flight day. Distinct signs of deconditioning developed on the 24th and 42d days. On these days, in spite of the decrease in amount of exercise, there was a substantial increase in HR, slower build-up of pedaling rate, elevation of AP and decrease in SV, as well as appearance of signs of diminished venous return. This stage of the flight was characterized by an increase in volume of work related to operation of the station, as a result of which there was a certain disruption of the work and rest schedule and, in particular, a decrease in physical exercise, as compared to the planned amount. Subsequent improvement of regulation of the cardiovascular system with the load on the 70th and 82d days was obtained by increasing the intensity of exercise with optimization of the work and rest schedule. Analogous findings were also made previously [1, 3].

Thus, the test on a bicycle ergometer enabled us to demonstrate deterioration of the reaction of the cardiovascular system to a physical load. Maximum changes were observed by the end of the 1st and start of the 2d month, whereas at the end of the flight the reaction was close to the preflight level. The poorer regulation of circulation was related primarily to deconditioning, due to an inadequate amount of physical exercise. It is imperative to implement the entire complex of preventive measures to maintain a high level of fitness.

BIBLIOGRAPHY

1. Rudnyy, N. M.; Gazenko, O. G.; Gozulov, S. A.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1977, pp 33-41.

2. Doroshev, V. G.; Batenchuk-Tusko, T. V.; Lapshina, N. A.; et al. Ibid, No 2, pp 26-31.

3. Degtyarev, V. A.; Doroshev, V. G.; Kalmykova, N. D.; et al. Ibid, No 3, 1978, pp 15-20.

4. Bergman, S. A.; Hoffler, G. W.; and Johnson, R. L. in "Skylab Life Symposium. Proceedings," Houston, Vol 11, 1974, pp 255-283.

5. Michel, E. L.; Rummel, J. A.; Savin, Ch. F.; et al. Ibid, pp 297-336.

6. Degtyarev, V. A.; Doroshev, V. G.; Kalmykova, N. D.; et al. KOSMICHESKAYA BIOL., No 2, 1974, pp 34-42.

7. Kukolevskiy, G. M. in "Serdtse i sport" [The Heart and Sports], Moscow, 1968, pp 303-331.

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HEMODYNAMICS AND PHASE STRUCTURE OF THE CARDIAC CYCLE IN MEMBERS OF THE FIRST CREW OF SALYUT-5 AT REST

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[Article by V. A. Degtyarev, V. G. Doroshev, N. A. Lapshina, V. N. Ragozin, Z. A. Kirillova, S. I. Ponamarev and O. B. Kulikov, submitted 6 Jul 79]

[English abstract from source]

In the Salyut-5 flight studies of circulatory functions were continued. Heart rate, arterial pressure, time intervals of the left and right ventricles were measured at rest. Peripheral resistance and cardiac output were calculated. At early flight stages cardiovascular changes occurred due to an increased blood inflow to the heart. During the second half of the mission cardiac output and arterial pressure remained elevated, as fatigue of the cosmonauts increased.

[Text] The study of circulation at rest in the first crew of the Salyut-5 orbital station is a continuation of the programs dealing with the study of the effects of space flight factors on the human body [1, 2]. In spite of the fact that a certain amount of data has been accumulated [3-6], the distinctions of hemodynamic changes in weightlessness require further investigation. This is attributable to the fact that each successive flight is experimental and contains new elements. There are changes in the cyclogram of crew work, work and rest schedule, conditions under which experiments are conducted, scope thereof, etc. As in all experimental work, elements of risk are retained. All this makes it difficult to interpret data and single out the specific changes that are related to the direct effect of weightlessness. Adherence to standard examination conditions, which could provide for good comparability of findings from studies conducted at different stages of a flight, constitutes an extremely difficult task.

Methods

Polynome-2M equipment was used for morning, daytime and evening studies before conducting functional tests involving lower body negative pressure (LBNP) and a physical load. Data were obtained for the flight engineer under basal metabolic conditions on the 40th day of the flight. The second crew member placed the sensors and adjusted equipment 20-30 min before the start of a telemetric communication session. A record was taken of the tachooscillogram of the brachial artery, kinetocardiogram (KKG) from the region of the apex beat and 4th intercostal space on the right, near the sternum, and sphygmogram of the femoral artery. We determined the heart rate (HR), minimum (AP_m), mean (AP_a), lateral (AP_l) and end (AP_e) systolic arterial pressure, pulse wave velocity (PWV) in the aorta, duration of isometric contraction (IC) and period of ejection (E) of blood by the ventricles, as well as interphase coefficient K [3]. We used the Bremse-Ranke formula to calculate stroke and minute volumes (SV, MV), and the method of N. N. Savitskiy [7] for determination of actual and working (proper) peripheral resistance (APR, WPR).

Results and Discussion

The distinctive feature of the cosmonauts' mission was that they performed very intensive work. The cosmonauts worked more on their own initiative than provided in the program. This resulted in reduction of time reserved for rest, meals and physical exercise. As a result, the crew members developed considerable fatigue, which was associated with substantial sleep disorders. Overall shortage of sleep constituted more than 100 h for both cosmonauts during the 49-day mission.

HR did not exceed preflight levels in the commander after the 4th day of the flight, whereas in the flight engineer it was lower by a mean of 8% than the initial level for the first 2 weeks of the mission and later exceeded the initial level by a mean of 29% (Table). We know from the prior flights that AP levels, particularly AP_l and AP_e, usually were 10-15 mm Hg higher for the first 2 weeks. Thereafter, as the cosmonauts adjusted to weightlessness, AP had a tendency toward normalization [1-3, 5, 6]. The commander's AP did not drop during the flight. The increment of AP_a and AP_e constituted a mean of 11% during the flight and AP_l 23%. In most cases, AP_m corresponded to the preflight level. The greatest elevation of all AP levels of the commander was observed on the 14th flight day, when he performed the work program of both crew members by himself. In the flight engineer, AP_m and AP_a remained at the prefight level, while AP_l and AP_e rose by a mean of 15%. Pulse pressure rose by a mean of 35% in both cosmonauts. The circulatory changes we observed resembled, to some extent, the dynamics of HR and AP of the commander of the Salyut-1 spacecraft and several American astronauts [1, 3, 6]. Berry [9] attributed this to the so-called "commander effect." He believed that the more frequent elevation of AP in spacecraft commanders was related to their special responsibility for performance of the

program of the mission. Unfortunately, American researchers do not measure SV and MV in weightlessness.

Hemodynamic parameters of resting Salyut-5 crew members

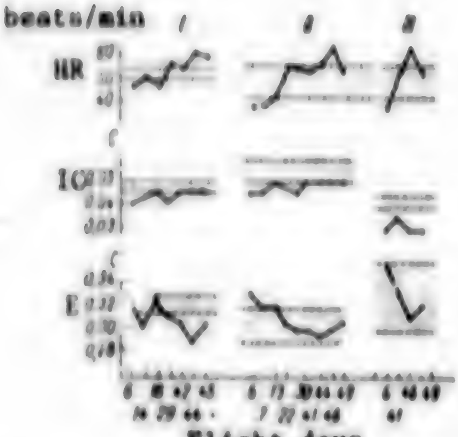
Time of study	HR	AP_m	AP_a	AP_l	AP_e	PWV, m/s	SV, mℓ	MV, ℓ	APR, arbitr. units
Commander									
Before flight	50	50	86	105	128	6,4	105	5,2	31
Flight days:									
6th	47	54	96	119	146	6,3	157	7,6	25
14th	50	70	96	132	153	6,9	135	6,7	27
16th	48	63	94	125	140	6,1	160	7,7	25
28th	56	65	96	126	148	6,5	145	8,1	23
46th	53	67	92	121	147	7,0	118	6,3	27
After flight (4th day)	59	63	90	113	132	5,9	130	7,6	22
Flight engineer									
Before flight	44	50	73	90	116	5,3	102	4,5	102
Flight days:									
6th	40	48	75	109	131	6,5	138	5,5	26
7th	41	48	72	100	132	6,6	121	5,0	27
13th	41	51	87	110	137	6,3	134	5,5	30
21st	55	48	—	98	130	6,0	128	7,0	—
28th	51	50	80	[illegible]	140	5,8	[illegible]	7,0	22
40th*	53	42	75	100	122	5,2	166	8,8	18
43d	58	57	79	108	132	6,1	121	7,0	26
After flight (4th day)	52	62	112	138	4.7	162	8,4	20	

Note: The asterisk refers to data obtained under basal metabolic conditions.

In the first month of the flight, the commander's SV was a mean of 46% greater than the preflight value and MV was 30% greater. It is only by the 46th day that circulation volumes decreased significantly, although they did not reach preflight levels. In the flight engineer, SV was 20% or more above the preflight level. For the first 2 weeks, MV was 10-20% above the preflight level. Thereafter, the differences constituted up to 50%.

In the commander, PWV remained in the range of preflight levels. In the flight engineer, the highest PWV was found at the first stage of the flight. From the 13th flight day on, PWV gradually decreased, remaining higher, on the average, than the preflight level.

APR of the commander decreased by 15% during the flight; however, the difference between APR and WPR exceeded +15% up to the 27th flight day, which was an indirect indication of some increase in arteriolar tonus. On the 44th day, APR conformed with the proper level. In the flight engineer, it was the same as before the flight for the first 2 weeks of flight, then decreased by 30%. On the 7th and 40th flight days, the difference between APR and WPR constituted 17%, i.e., vascular tonus was decreased on these days.



Dynamics of phases of the left ventricle for commander (I) and flight engineer (II), and right ventricle for flight engineer (III) during flight. The striped area indicates the range of preflight figures

The shape of the KKG of the apex of the heart and from the 4th intercostal space to the right of the sternum corresponded to the findings on the ground. There were two stages of changes in phase structure of the cardiac cycle. The first stage (6th-16th days for the commander and 6th-13th days for the flight engineer) was characterized by some slowing of the pulse, longer period of ejection and mechanical systole of the left ventricle in relation to proper values. Coefficient K changed particularly distinctly in the flight engineer due to some extension of the ejection period and shortening of the period of isovolumetric contraction (see Figure). Examination of phases of the right ventricle of the flight engineer, made on the 6th flight day, yielded analogous findings.

At the second stage, starting on the 22d flight day, the flight engineer presented reduction of ejection period and mechanical systole to the bottom preflight range against the background of higher HR. In the commander, the ejection period and mechanical systole decreased even more starting on the 29th day; however, the duration of these phases in both cosmonauts virtually corresponded to the proper values. The duration of isometric contraction and coefficient K increased, as compared to the first stage of the flight. Examination of duration of right ventricular phases in the flight engineer at the end of the flight (41st, 46th and 49th days) also revealed shortening of the ejection period and mechanical systole, as compared to the values obtained at the start of the flight.

Evidently the differences in dynamics of circulatory parameters of the crew members were attributable to their individual adaptability to the drastically changing working conditions on the station. During the period between the 21st and 30th days, when the "sleep-waking" cycle was shifted by almost 6 h in both directions, the commander developed a vegetovascular crisis [8]. Thereafter, additional rest time was granted to the crew, and the commander was able to sleep for 30-40 min in the daytime. As a result, the cosmonaut felt better. By the end of the mission, his circulation volume decreased substantially. There was no normalization of impaired sleep for the flight engineer. Signs of fatigue progressed, and headache was added to them. Perhaps, deterioration of general condition and diminished fitness for work in the flight engineer were due to the

disturbances in regulation of vascular tonus. Examination of the cosmonaut at this time revealed great lability of AP and a substantial increase in MV, that were inconsistent with his state of rest. Even under close to basal metabolic conditions (40th day), SV and MV were significantly higher than preflight levels. PWV decreased, while the difference between APR and WPR exceeded 15%, which was indicative of relative decrease in vascular tonus. A comparison of rheographic data on the 26th and 46th flight days revealed an increase in venous components and signs of decreased arterial tonus in the fronto-occipital lead in the light engineer. During this period, he had less endurance for the functional tests with exercise and LBNP.

Thus, the first crew of Salyut-5, unlike all crews that had previously flown aboard orbital stations, presented relatively greater elevation of circulatory indices in weightlessness, without overt regression with increase in duration of the flight. With constant exposure to space flight factors, the marked circulatory reaction, inconsistent with rest, probably reflected the cosmonauts' increasing fatigue and development of close to pathological states. The obtained data expand existing conceptions of the distinctions and criteria for evaluating adjustment of cosmonauts at different stages of flight.

BIBLIOGRAPHY

1. Degtyarev, V. A.; Doroshev, V. G.; Kalmykova, N. D.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1974, pp 34-42.

2. Doroshev, V. G.; Batenchuk-Tusko, T. V.; Lapshina, N. A.; et al. Ibid, No 2, 1977, pp 26-31.

3. Degtyarev, V. A.; Popov, I. I.; Batenchuk-Tusko, T. V.; et al. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 132-157.

4. Degtyarev, V. A.; Doroshev, V. G.; Batenchuk-Tusko, T. V.; et al. KOSMICHESKAYA BIOL., No 3, 1977, pp 26-31.

5. Itsekhovskiy, O. T.; Polyakova, A. P.; and Lyamin, V. R. Ibid, No 2, pp 37-42.

6. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. N.; et al. Ibid, No 5, 1976, pp 3-18.

7. Savitskiy, N. N. "Biophysical Bases of Circulation, and Clinical Methods of Studying Hemodynamics," Leningrad, 2d edition, 1963.

8. Rudnyy, N. M.; Gazenko, O. G.; Gozulov, S. A.; et al. KOSMICHESKAYA BIOL., No 5, 1977, pp 33-41.

9. Berry, Ch. A. in "Man in Space," Moscow, 1974, pp 51-70.

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EFFECT OF WEIGHTLESSNESS AND ARTIFICIAL GRAVITY ON ION-REGULATING FUNCTION OF RAT KIDNEYS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 21-25

[Article by Ye. A. Il'in, Yu. V. Natochin, N. A. Ilyushko, Yu. I. Kondrat'yev, V. T. Bakhteyeva, Ye. M. Gazhala, O. A. Goncharevskaya, Ye. A. Lavrova and Ye. I. Shakhmatova, submitted 13 Feb 79]

[English abstract from source]

Weightless rats showed greater changes in the fluidelectrolyte metabolism and ion regulatory function of the kidneys than centrifuged rats. During water loads they exhibited an increased sodium excretion. During potassium loads they displayed a higher potassium excretion. The study of electrolyte composition of different kidney segments demonstrated a reduced potassium content in the wet cortical and medullary matter due to elevated tissue hydration. Kidney microdissection did not reveal any structural differences in nephrons of the weightless and centrifuged rats.

[Text] Man's exposure to space flight conditions is associated with significant changes in fluid-electrolyte metabolism and renal function [1-3]. Studies involving the use of functional load tests revealed substantial changes in systems of regulation of fluid-electrolyte metabolism in man under weightless conditions [7].

In this article, we studied the reaction of kidneys and systems of their regulation to a water and potassium load, we measured the electrolyte composition of different parts of the kidney and performed microdissection of the kidney in experiments on rats aboard Cosmos-936 biosatellite, for the purpose of analyzing the physiological mechanisms of the effect of weightlessness on ion-regulating renal function.

Methods

We used in the experiment 15 Wistar SPF rats (5 rats were submitted to weightlessness, 5 to artificial gravity, and a synchronous control

experiment was conducted with the other 5). The flight and synchronous experiments lasted 18.5 days. All three groups of animals were fed the same diet of feed in paste form at the rate of 40 g/day.

Tests with a water load (5 mℓ/100 g weight) were conducted on the 1st and 4th days after the flight and synchronous experiments, and tests with a load of 1.25% KCl solution (5 mℓ/100 g weight) on the 2d and 5th days. After the water and salt loads, urine was collected every 30 min for 4 h. We assayed in all urine samples the concentration of sodium and potassium using a flame photometer, calcium and magnesium concentration using an atom-absorption spectrophotometer. Studies of electrolyte composition of different parts of the kidney (cortex, external medullary layer, renal papilla) were made after ashing the samples with concentrated HNO_3. For microdissection of the kidney, it was macerated in HCl, then whole superficial, intracortical and juxtamedullary nephrons were isolated.

Results and Discussion

Elimination of water load: The test with a water load was conducted to evaluate the osmoregulatory system and possible fluid deficiency in the organism. Elimination of the water load was at a maximum in rats submitted to weightlessness, on the first day after the experiments (Figure 1). On the 4th day of the recovery period, fluid elimination after the water load was reliably lower in flight animals than those of the synchronous experiment. A comparison of the dynamics of development of the diuretic reaction and level of maximum diuresis in the three groups of animals failed to demonstrate reliable differences.

Analysis of ionograms of urine after the water load is of substantial significance to evaluation of the condition of the kidneys and osmoregulatory system. In rats that had been submitted to weightlessness, we demonstrated maximum elimination of sodium (see Figure 1) on the 1st day of the readaptation period. We failed to demonstrate differences in elimination of potassium, calcium and magnesium in the three groups. On the 4th day of the readaptation period, elimination of sodium and potassium after the water load was reliably lower in flight rats than in animals used in the synchronous experiment.

Elimination of potassium load: The studies of excretion of potassium loads after a space flight, which were conducted on animals for the first time, were of great interest to characterization of potassium metabolism. Intake of potassium led to virtually the same increase in elimination of fluid in animals involved in the flight and synchronous experiment (Figure 2). On the 5th day of readaptation, excretion of fluid after the potassium load was reliably lower in flight animals than those in the synchronous experiment. On the 2d day of readaptation, excretion of potassium was highest in flight animals exposed to weightlessness. On the 5th day after landing there were no differences between all three groups with regard to excretion of potassium after a potassium load (see Figure 2).

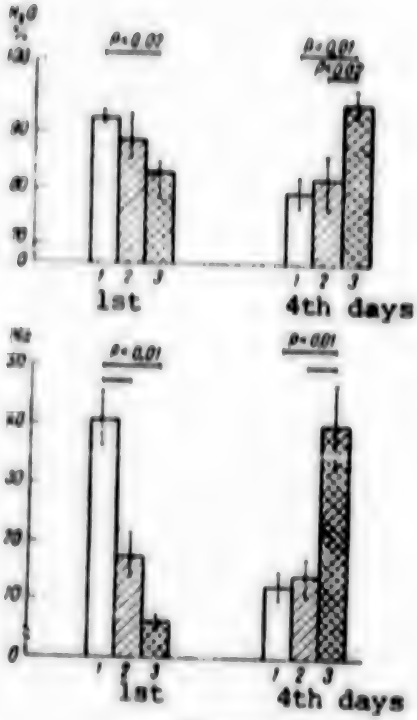

Figure 1.
Excretion of fluid (% of given volume) and sodium (in μeq/100 g weight in 4 h) after water load

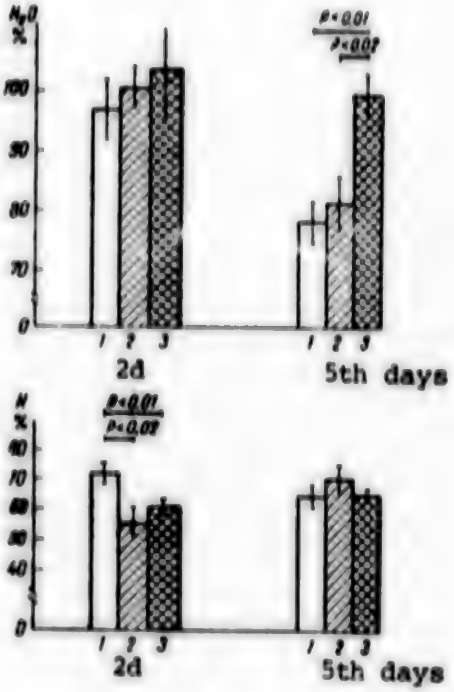

Figure 2.
Excretion of fluid (% of given volume) and potassium (% of given quantity) after potassium load

Key to both figures:
1) flight, weightlessness 2) flight, centrifuge 3) synchronous experiment

Excretion of sodium, potassium and magnesium after a potassium load was virtually the same in all three groups of animals on the 2d day of the readaptation period. On the 5th readaptation day, excretion of sodium was reliably lower in flight animals than those of the synchronous experiment.

Microdissection of the kidney: It can be assumed that the above-mentioned changes in renal reactions to the tests are related either to structural and biochemical changes in renal tissue, or change in regulatory mechanisms. Hypotheses have been expounded previously that space flights can lead to stasis in urinary tubules and deformation thereof. For this reason, we performed microdissection of the kidneys and isolated nephrons. The obtained results failed to demonstrate any differences whatsoever in structure of different parts of neprhons of all populations after the flight.

Electrolyte composition of different parts of the kidney: Assay of sodium and potassium in the cortex and medullary substance of the kidney enabled us to determine the gradient created by the function of the

reflux system and to tentatively evaluate the changes in cellular concentration of potassium, since tissular potassium is determined primarily by the level of cellular potassium. The most substantial differences were found in potassium content of different parts of the kidney (see Table). After exposure to weightlessness, it was reliably lower (as compared to indices for the synchronous experiment) in wet cortical substance ($P<0.001$), external and internal (papilla) medullary substance ($P<0.01$). The changes were less marked in rats kept in a centrifuge during the flight than in control animals. They were not demonstrable in the renal cortex, but only found in the medullary layer ($P<0.05$).

Electrolyte composition of different parts of the kidney (M±m)

Region of kidney	Flight--weightlessness		Flight--centrifuge		Synchronous experiment	
	day of study					
	1	25	1	25	1	25
H_2O (kg/kg dry substance)						
Cortex	3,1±0,1		2,96±0,09		2,8±0,06	
Medullary substance (external zone)	4,28±0,3		3,96±0,05		3,54±0,11	
Papilla (internal zone)	5,95±0,34		5,94±0,19		5,5±0,25	
Na (meq/kg wet substance)						
Cortex	65,4±2,2	72,4±8,7	65,2±2,5	55,4±5,5	59,2±2,9	63,8±1,9
Medullary substance (extern.)	102,6±5,8	76,9±5,1	113,7±4,8	81,8±5,3	72,4±2,6	86,5±4,9
Papilla (intern.)	124,8±6,8	96,1±8,2	156,8±6,0	88,9±6,4	125,4±12,0	99,2±4,0
Na (meq/kg dry substance)						
Cortex	267,5±7,4		260,6±14,9		225,8±12,5	
Medullary substance (extern.)	538,0±30,3		573,2±20,9		329,0±15,4	
Papilla (intern.)	884,2±40,0		1091,2±58,6		752,6±38,9	
K (meq/kg wet substance)						
Cortex	70,6±1,0	74,6±2,5	78,1±1,8	77,2±2,2	79,2±0,2	73,3±1,9
Medullary substance (extern.)	63,6±3,3	68,0±1,4	68,9±2,6	70,9±2,6	76,6±0,95	74,6±6,1
Papilla (intern.)	58,6±5,4	66,8±4,3	71,9±2,9	60,3±1,2	81,5±3,0	65,4±2,3
K (meq/kg dry substance)						
Cortex	289,8±10,7		310,8±4,2		300,6±4,2	
Medullary subst. (external)	332,0±9,3		346,7±15,2		347,8±5,5	
Papilla (intern.)	450,0±48,0		494,7±34,0		532,6±32,7	

Analysis revealed that the cause of decrease in concentration of potassium in different parts of the kidney is increased hydration of renal tissue, since potassium content did not change when scaled to dry substance (see Table). The change in cellular potassium concentration could be one of the causes of increased natriuresis in rats during the period of the water load, since a shortage of potassium diminishes reabsorption of sodium by cells of the thick ascending limb of Henle's loop [8].

The main finding of prior studies of fluid-electrolyte metabolism in experiments aboard Cosmos biosatellites was that there was a lower percentage of water input excreted by the kidney than after the synchronous experiment, while sodium and potassium balance was positive [4, 6]. The results of that study warrant the belief that the lower percentage of fluid excreted by the kidney on the 1st postflight day, in relation to fluid intake, is not related to fluid retention in the organism, but to a different level of extrarenal loss. Perhpas, this is due to increased expenditure of fluid in the postflight period by the rats to lick their coats, which was difficult to do when they were kept in the automated life support systems and under weightless conditions [6].

A comparison of the reaction of the human kidneys to a water load after a space flight and with simulation of weightlessness (prolonged hypodynamia with bed rest in antiorthostatic [head down] position) shows that there is fluid retention in both cases [1, 3]. The cause of differences in reactions to a water load of man and animals on the first day of the readaptation period is that there is very marked redistribution of fluid in man, because of his vertical body position, after he returns to his usual surroundings, and this is one of the important factors in fluid retention. In view of the horizontal position of great vessels in rats, such a reaction is not observed. The decreased fluid output after a water load in animals participating in the flight, on the 4th postflight day is apparently related to maximum retention of electrolytes at this stage of the study. Thus, maximum retention of sodium, potassium and calcium was noted on the 4th-5th day after the experiment aboard Cosmos-605 and on the 3d day of readaptation after the one aboard Cosmos-782.

Hypokalemia and a negative potassium balance develop in man when he remains in antiorthostatic position (simulation of weightlessness) for a long time. Under such conditions, the potassium load is eliminated faster, in spite of the potassium deficiency [7]. Such a phenomenon was also observed in rats after termination of the space flight experiment. These data indicate that a potassium load can be used to evaluate the body's ability to deposit potassium. With decrease in capacity of the depot (perhaps due to atrophy of muscle cells), potassium excretion increases, and this is demonstrable after the flight.

Thus, the greatest changes in fluid-electrolyte metabolism and ion-regulating function of the kidneys after the experiment aboard Cosmos-936 were

noted in rats that were weightless during the flight. After a water load on the first day of readaptation, these animals presented increased sodium excretion. With a potassium load on the 2d postflight day, potassium excretion was at a maximum also in rats that had been submitted to weightlessness. Analysis of electrolyte composition of different parts of the kidney revealed a decrease in potassium content of wet cortical substance and medullary substance of the kidney, which is apparently due to increased tissular hydration. Microdissection of the kidney failed to demonstrate structural differences in nephrons of animals in different groups.

BIBLIOGRAPHY

1. Natochin, Yu. V.; Kozyrevskaya, G. I.; and Grigoryev, A. I. ACTA ASTRONAUT., Vol 2, 1975, pp 175-188.

2. Whedon, D.; Lutwaki, L.; Reid, I.; et al. Ibid, pp 297-309.

3. Grigor'yev, A. I.; Kozyrevskaya, G. I.; Natochin, Yu. V.; et al. in "Kosmicheskiye polety na korablyakh 'Soyuz'" [Space Flights Aboard the Soyuz Series Craft], Moscow, 1976, pp 226-234.

4. Ilyushko, N. A.; Il'in, Ye. A.; Kondrat'yev, Yu. I.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1977, pp 23-26.

5. Ilyushko, N. A.; Il'in, Ye. A.; Korol'kov, V. I.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 1, 1975, pp 12-14.

6. Ilyushko, N. A., and Kondrat'yev, Yu. I. "Trudy 8-kh chteniy, posvyashch. razrabotke nauchnogo naslediya i razvitiyu idey K. E. Tsiolkovskogo. Sektsiya 'Problemy kosmicheskoy meditsiny i biologii'" [Transactions of 8th Lectures Dedicated to Development of the Scientific Legacy and Ideas of K. E. Tsiolkovskiy. Section on "Problems of Space Medicine and Biology"], Moscow, 1974, pp 96-106.

7. Grigor'yev, A. I.; Dorokhova, B. R.; Kozyrevskaya, G. I.; et al. FIZIOLOGIYA CHELOVEKA [Human Physiology], No 4, 1979, pp 660-669.

8. Maxwell, M., and Kleeman, C. R. (editors) "Clinical Disorders of Fluid and Electrolyte Metabolism," New York, 1972, p 638.

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ACTIVITY OF SOME HEPATIC ENZYMES AND LIPOGENETIC PROCESSES IN RAT ADIPOSE TISSUE AFTER SPACE FLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 26-29

[Article by L. Makho, Sh. Nemet, M. Palkovich, V. Shtrbak and R. A. Tigranyan, submitted 17 Aug 78]

[English abstract from source]

The rats flown aboard Cosmos-782 showed a significant increase in the activity of tyrosine aminotransferase and tryptophan pyrolase, i. e. the enzymes whose activity depends on the corticosterone level. The synchronous rats displayed a small increase in the enzyme activity. The flight and synchronous animals exhibited a slight increase in the activity of gluconeogenetic enzymes and a decrease in the activity of glucose-6-phosphatase. Immediately after flight and, to a lesser extent, after the synchronous experiment the activity of lipogenetic enzymes decreased. On the R+25 day the enzyme activity remained unchanged. The study of lipogenesis in the epididymal fat, using C^{14}-glucose incorporation into lipids, did not reveal any differences in the flight and synchronous rats. The findings demonstrated that changes in the enzyme activity induced by the flight and synchronous experiments returned to the normal during readaptation.

[Text] Studies conducted in experiments aboard the Cosmos series of biosatellites revealed that prolonged weightlessness of rats leads to changes in some physiological functions, morphological state of organs and impairment of metabolic processes [1-6]. Morphological signs were demonstrated of increased functional activity of the hypothalamo-hypophyseo-adrenal system (HHAS) [1] and increased corticosterone concentration in blood plasma [5], which are indicative of a stress state due to the space flight factors. The space flight led to weight loss of the animals and decrease in adipose tissue in the subcutaneous fat and fat depots [3].

Our objective was to study the activity of some enzymes of the liver as related to corticosterone level in plasma, as well as enzymes of lipogenesis in the liver and processes of lipogenesis in adipose tissues of rats following a space flight.

Methods

The studies were conducted on male Wistar SPF rats 6-10 h and 26 days after a 19.5-day experiment aboard Cosmos-782. The obtained data were compared to the results of studies of animals in a synchronous experiment and vivarium control. To determine enzyme activity, liver specimens from animals sacrificed right after the flight were immediately frozen in liquid nitrogen and transported to the laboratory in a frozen state. Tissue homogenates were analyzed for activity of the following: tyrosine aminotransferase (TAT) [7], tryptophan pyrrolase (TP) [8], alanine aminotransferase (ALT) and asparate aminotransferase (AST; by the Farb Test method, Boeringer, Mannheim), phosphoenopyruvate carboxykinase (PEPCK) [9], fructose diphosphatase (FDP) [10], glucose-6-phosphatase (G6P) [11], malic enzyme [malate dehydrogenase] (ME) [12], glycerol phosphate oxidase (GP) [13], ATP citrate lyase [14] and serine dehydrase (SD) [15]. Protein was assayed by the method of Lowry et al. [16]. After the readaptation period (i.e., 26th day after landing), determination was also made of radioactive carbon-labeled glucose uptake in lipids of adipose (epididymal) tissue [17] and in the lipid fraction after separation by thin-layer chromatography [17].

Results and Discussion

Figures 1 and 2 illustrate data on activity of enzymes of amino acid metabolism in the liver of control and flight animals. A significant increase in TAT and TP activity was demonstrated in rats involved in the 19.5 day flight and sacrificed 6-10 h after termination thereof. The activity of these hepatic enzymes is very dependent on adrenocortical hormone level, and it increases already after one injection of corticosterone [18, 19]. Some increase in activity of both hepatic enzymes was demonstrated in rats used in the synchronous experiment.

TP activity in the liver of rats used in the flight and synchronous experiments 26 days after the flight did not differ from its activity in the control group, whereas TAT activity was lower in flight animals than the control. In the second half of the experiment, control animals presented high TAT activity in the liver.

Determination of ALT, AST and SD activity revealed that, immediately after the flight, AST activity was higher than in rats of both control groups; ALT and SD activity after the flight and synchronous experiments showed virtually no difference from that of animals in the vivarium control (see Figures 1 and 2).

After lengthy weightlessness, we observed only a minor increase in FDP and PEPCK activity (see Figure 2); FDP activity was also higher in the synchronous experiment. In the first hours after the flight and synchronous experiment there was a decrease in G6P activity; however, during the

readaptation period, the activity of this gluconeogenetic enzyme increased reliably in both groups of animals, as compared to control levels (see Figure 2).

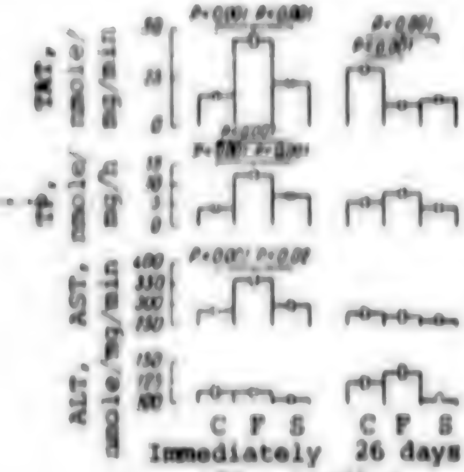

Figure 1.
TAT, TP, AST and ALT activity in rat liver. Here and in Figure 2:
- C) control
- F) flight
- S) synchronous experiment

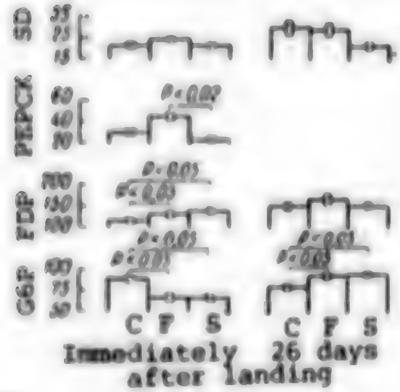

Figure 2.
SD, PEPCK, FDP and G6P activity in rat liver (nmole/mg/min)

The obtained results warrant the conclusion that there is an increase in processes of gluconeogenesis in animals used in the flight and synchronous experiments. The decrease in G6P activity in the first hours after the flight indicates that the glucose synthesized in the process of gluconeogenesis is utilized mainly for glycogen synthesis in the liver; but, in view of increased activity by the end of the readaptation period, G6P is released in a free form into the blood. There was significant increase in blood glucose concentration in rats sacrificed 6-10 h after the flight [5].

The concurrent increase in plasma corticosterone concentration after the flight [5] and elevation of blood glucose level are the result of inhibited utilization thereof, as was shown in other models of stress [20].

Determination of ME and ATP citrate lyase activity in the liver showed that it was significantly decreased immediately after the flight and in animals of the synchronous ground-based experiment. ME activity did not differ from the control 26 days after the flight and synchronous experiment (Figure 3). The obtained results indicate that keeping rats in the box-cages aboard the biosatellite and in the mock-up has an inhibitory effect on processes of biosynthesis of fatty acids. After the readaptation period, there is probable normalization of hepatic lipid biosynthesis. The change in ME activity is unrelated to the influence of thyroid hormones, since GP activity does not change after the flight, and this enzyme is very sensitive to thyroxine [13].

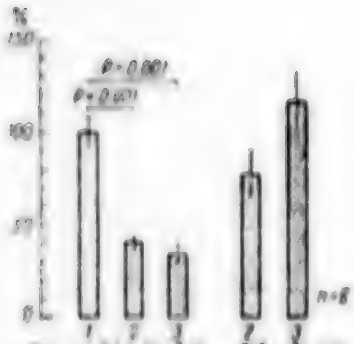

Figure 3.
MF activity in rat liver (% of control). Here and in Figure 4:
1) vivarium control
2) synchronous ground-based experiment
3) flight

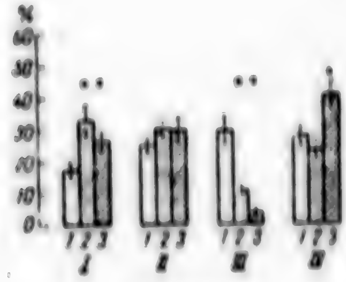

Figure 4.
Glucose uptake in adipose tissue lipid fraction
I) "start" fraction
II) mono- and diglycerides
III) fatty acids
IV) triglycerides
*) P<0.01, as compared to control

After readaptation to earth's gravity, flight animals failed to demonstrate reliable differences in rate of lipid biosynthesis in adipose tissue. However, separation of lipids into fractions (Figure 4) revealed that, in flight rats, there is significant uptake of glucose in the triglyceride and "start" fractions (probably, polar lipids, phospholipids), as a result of which there is a decrease in fatty acid fraction.

A comparison of the results of determination of activity of enzymes of amino acid metabolism and gluconeogenesis in the rat liver after the flight, as well as with acute and recurrent stress [18, 19], revealed that experimental animals presented an increase primarily in activity of enzymes (PEPCK, TAT, TP), the amount of which increased already after a single injection of corticosterone [18]. However, the activity of enzymes, the amount of which in the liver increases only after repeated injection of corticosteroids or after repeated stress [19], did not differ in animals after the space flight and ground-based synchronous experiment, as compared to control levels.

The obtained data indicate that the increase in activity of the HHAS and hepatic enzymes is primarily the result of the effects of the set of factors of acute stress during the final stage of the experiment, while prolonged weightlessness does not induce the same changes as repeated stress does in activity of hepatic enzymes [18, 19]. There was a decrease in activity of lipogenetic enzymes of the liver and fatty acid synthesis in weightless rats and those of the synchronous experiment. In spite of this, the rats in the flight and synchronous experiment groups presented an increase in concentration of triglycerides in the liver and

nonesterified fatty acids in plasma and adipose tissue [6]. It may be assumed that increased lipid mobilization in adipose tissue is the cause of increase in nonesterified fatty acids and triglycerides of the liver, although processes of lipogenesis were diminished in this organ. By the end of the readaptation period, the indices of activity of lipogenetic enzymes of the liver were essentially restored to normal. Uptake of glucose in total lipids of experimental animals also failed to differ from the intact control; however, after completion of the flight, there was increase in incorporation of glucose in triglycerides and the fraction with phospholipids in adipose tissue. It may be assumed that glucose is incorporated in these molecules of lipid fractions chiefly in the form of glycerol. In the future, it will be necessary to pay attention to these changes in lipid metabolism of adipose tissue of animals used in space flights and ground-based model experiments.

BIBLIOGRAPHY

1. Portugalov, V. V.; Savina, Ye. A.; Kaplanskiy, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1976, pp 19-25.

2. Gazenko, O. G.; Demin, N. N.; Panev, A. N.; et al. Ibid, pp 14-19.

3. Il'in, Ye. A.; Serova, L. V.; and Noskin, A. D. Ibid, No 3, pp 9-14.

4. Gayevskaya, M. S.; Ushakov, A. S.; Belitskaya, R. A.; et al. Ibid, No 4, pp 25-30.

5. Tigranyan, R. A.; Popova, I. A.; et al. in "Simpozium po kosmicheskoy biologii i meditsine. 9-y. Tezisy dokladov" [Summaries of Papers Delivered at the 9th Symposium on Space Biology and Medicine], Budapest, 1976, p 83.

6. Alers, I.; Tigranyan, R. A.; et al. Ibid, p 96.

7. Diamondstone, T. L. ANALYT. BIOCHEM., Vol 16, 1966, pp 395-401.

8. Knox, W. E., and Auerbach, V. H. J. BIOL. CHEM., Vol 214, 1955, pp 307-313.

9. Nordlie, R. C., and Lardy, H. A. Ibid, Vol 238, 1963, pp 2259-2263.

10. Taketa, K., and Pogell, B. M. Ibid, Vol 240, 1965, pp 651-662.

11. Harper, A. E., and Bergmayer, M. W. in "Methods of Chemical Analysis," Weinheim, 1962, p 788.

12. Ballard, F. J., and Hanson, R. W. BIOCHEM. J., Vol 102, 1967, pp 952-958.

13. Hemon, P. BIOCHIM. BIOPHYS. ACTA, Vol 132, 1967, pp 175-178.

14. Srere, P. A. J. BIOL. CHEM., Vol 234, 1959, pp 2544-2547.

15. Goldstein, L., Knox, W. E.; et al. Ibid, V-1 237, 1962, pp 2855-2860.

16. Lowry, O. H.; Rosebrough, N. J.; Farr, A. L.; et al. Ibid, Vol 193, 1951, pp 265-275.

17. Macho, L., and Saffran, M. ENDOCRINOLOGY, Vol 81, 1967, pp 179-185.

18. Nemeth, S. LEK. OBZ., Vol 23, 1974, pp 359-363.

19. Idem, in "Hormones, Metabolism and Stress," Bratislava, 1973, pp 229-241.

20. Nemeth, S., and Vigas, M. ENDOCR. EXP., Vol 2, 1968, pp 179-184.

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STATE OF RAT THYROID C CELLS FOLLOWING FLIGHTS ON THE COSMOS TYPE OF BIOSATELLITES (ACCORDING TO RESULTS OF A MORPHOLOGICAL STUDY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 29-33

[Article by G. I. Plakhuta-Plakutina, submitted 28 Jan 79]

[English abstract from source]

Calcitonin-secreting cells (C-cells) of the thyroid glands from 51 SPF Wistar rats flown for 18.5 to 22 days aboard biosatellites Cosmos-605, 782 and 936 and sacrificed 4.5–13 hours, 1–2 and 25–27 days after recovery were examined histologically and karyometrically. Vivarium (57) and synchronous (58) rats were used as controls. Variations in the nuclear volume of C-cells and their density were shown to depend on the experimental conditions and time interval elapsed after recovery. Morphological changes in C-cells were assumed to be associated with alterations in calcium metabolism during an exposure of rats to weightlessness, artificial gravity and Earth gravity.

[Text] According to data in the literature, the hormone thyrocalcitonin secreted by thyroid C cells has a hypocalcemic action, which is the opposite of the action of parathyroid hormone, due to inhibition of resorptive processes in bone tissue [1-4], while an increase in number and size of C cell nuclei is indicative of increased calcitonin synthesis [5-8].

Previous studies of the rat thyroid after a flight aboard the Cosmos-605 biosatellite established a significant increase in calcitonin-secreting cells and morphological signs of increased functional activity thereof [9]. However, it was not possible to determine whether this phenomenon is related to space flight factors (in particular, weightlessness or the period of return to earth's gravity), since the animals were sacrificed 1-2 days after the flight, and the changes in both C cells and the thyroid proper could have been due to gravitational stress.

Since animals were sacrificed as soon as feasible after termination of the flights aboard Cosmos-782 and Cosmos-936, we were able to compare the results of histological and karyometric studies of thyroid C cells within the first 4.5-13 h and 2 days after long-term weightlessness.

Methods

The material studied consisted of thyroids from 15 male Wistar rats that had been aboard Cosmos-605 for a 22-day flight and 11 Wistar SPF rats that had spent 19.5 days aboard Cosmos-782. The distinctive element of the experiment conducted aboard Cosmos-936 was that artificial gravity simulating earth's gravity was created [10]. The thyroids of 15 rats that had spent 18.5 days in weightlessness and 10 kept on a centrifuge during the flight were submitted to examination. As a control for each of these flight experiments, we used an equal number of rats from ground-based model experiments, in which all space flight factors were simulated with the exception of weightlessness, as well as intact animals that remained in the vivarium throughout the experiment. The animals were decapitated 4.5-13 h and 1-2 days after the flight and termination of ground-based experiments, as well as after 25-27 days of the aftereffect period.

The excised thyroid (from a total of 166 rats) was fixed in Bouin fluid and imbedded in paraffin. The sections were stained with hematoxylin and eosin, as well as Heidenhain's azan. The colloid in the thyroid was stained according to Marais and Ham [11]. We used hematoxylin and luminous green, and impregnation with silver nitrate by the method of Grandi [12] to demonstrate C cells and assess their functional state.

C cells were counted using an ocular grid at magnifications of 40× for the objective and 7× for the ocular. C cell nucleus volume was measured using an RA-6 projection attachment [drafting machine] (MBI-11 microscope). At a linear magnification of 2000×, we drew the outline projections of 100 C cell nuclei from sections of thyroid from each animal, and determined the logarithms of their volumes using the formula for an ellipsoid of revolution [spheroid]:

$$V = \frac{\pi}{6} (LD)^{3/2}$$

and the nomograms of Fischer and Inke [13]. Subsequent calculations were made by the conventional karyometric methods of variational statistics [14]. The results were considered reliable with $P<0.05$. The reliability of differences was determined by the criterion of Student and Fisher.

Results and Discussion

A reliable decrease in number of C cells (by 18%) was demonstrated in rats taken from Cosmos-936, which had been weightless during the flight and were sacrificed within 4.5-9 h after the flight, as compared to the vivarium control ($P<0.01$).

The C cells presented mainly epifollicular localization, and they were not always clearly circumscribed with use of the ordinary staining methods. Impregnation of sections according to Grandi revealed that the C cells were

small, more often encountered alone and they seldom formed accumulations. With regard to secretory granule content, they were very similar: the granules were dark, fine and arranged in the form of narrow bands in the perinuclear region of the cytoplasm in most cells.

Karyometric studies revealed a substantial decrease in volume of C cell nuclei in flight group rats: by 32.6% as compared to the vivarium control (99.5±6.1 and 147.6 3.3 μm^3, respectively, $P<0.001$). The variational curve of logarithms of the volume of C cell nuclei was distinctly shifted to the left for rats in the weightless group, which was indicative of prevalence of small nuclei (Figure 1).

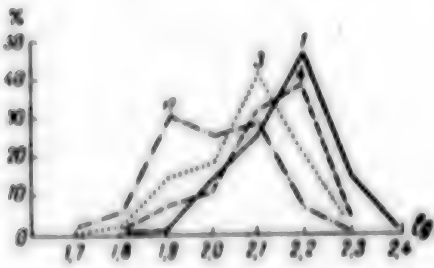

Figure 1.
Variational curves of logarithms of volume of thyroid C cell nuclei (Cosmos-936). X-axis, classes of nucleus volume (logarithms); y-axis, % nuclei in each class. Here and in Figure 2:

1) vivarium control
2) weightlessness
3) ground-based synchronous experiment
4) artificial gravity in flight

There was an increase in number of demonstrable parafollicular cells 9-11 h after flight (Cosmos-782), and the number was close to the control ($P\leq 0.05$), whereas the size of C cell nuclei did not yet reach control values (Figure 2).

Examination of thyroid tissue within 4.5-13 h after the flight revealed morphological signs of some decrease in function, as manifested by a decrease in height of follicular epithelium, consolidation of colloid and absence of resorption vacuoles. In addition, there was prevalence of follicles with yellow colloid, indicative of decrease in iodinated amino acid content of the colloid.

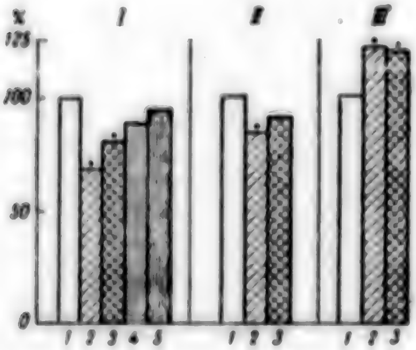

Figure 2.
Dynamics of changes in thyroid C cell nucleus volume. Vertical axis, C cell nucleus volume (% of control). The dots refer to reliable differences from control

I) Cosmos-936 (4.5-9 h after land-landing)
II) Cosmos-782 (9-11 h after land.)
III) Cosmos-605 (48 h. " ")
5) animals rotated in ground-based centrifuge at 1.4 G

We demonstrated a decrease in size of C cell nuclei ($118.6 \pm 2.3\ \mu m^3$), as is clearly seen in Figure 1, in rats from the ground-based experiment, which simulated flight conditions, as in animals submitted to weightlessness. The similar direction of changes in C cells in the compared groups warrants the belief that the decrease in number of C cells and morphological signs of depressed function thereof are related to the influence of weightlessness and hypokinesia.

In rats kept on a centrifuge during the flight, the histology of the thyroid differed from that of rats in the weightless group in that there were signs indicative of some increase in functional activity. The follicular epithelium was tall, cuboidal, and colloid was less dense than in rats submitted to weightlessness, often with fine marginal vacuoles; its tinctorial properties did not differ from those of colloid of intact animals. Interfollicular tissue was represented by proliferative islets, among which parafollicular cells were often encountered. The latter, according to degree of cytoplasmic granulation, were at different stages of the secretory cycle. The population of C cells of rats put on the centrifuge was considerably larger than in the group of rats submitted to weightlessness (by 37%; $P<0.001$), but close to the population size in animals from the vivarium control ($P<0.05$). The C cell nucleus volume constituted $131.3 \pm 6.3\ \mu m^3$, and it did not differ from the control with statistical reliability (see Figures 1 and 2).

In rats from Cosmos-605 examined 48 h after the flight, we found morphological signs of activation of the thyroid, manifested by capillary plethora, epithelial polymorphism, clearing and vacuolization of apical ends of the thyrocytes, liquefaction and resorption of colloid. Visual examination of preparations revealed impressive increase in number and size of C cells, which were encountered chiefly in the central parts of the gland, isolated in the walls of follicles or in groups of 4-6 cells in interfollicular tissue. A count of the C cells revealed a significant increase in their number (by 92.3%) and nuclear volume (by 22%); we also observed varying degrees of cytoplasmic degranulation on sections impregnated by the Grandi method more often than in control animals.

The histological structure of the thyroid of rats in the flight group did not differ from that of animals from the corresponding ground experiments and vivarium control 25-27 days after completion of the flight. The morphological features of the C cells also failed to demonstrate differences from the control, but their number remained high and was 13% above the control level.

Analysis of morphometric data for C cells of animals flown aboard the biosatellites and sacrificed at different times after the flights revealed that the transition from weightlessness to earth's gravity is a powerful stimulus for activation of the C cell system. Indeed, it was logical to expect a reaction from the calcitonin-secreting cells, the hormone of which, as we know, reduces elimination of calcium from bones and inhibits

resorption of the bone matrix [15, 16], while morphological signs of functional changes are manifested quite rapidly, within a few hours to 1 day [17-19].

Within the first few hours after the flight, there was a decrease in number and size of C cells, with signs of decreased functional activity, against the background of some signs of hypofunction, which were also noted in the gland's parenchyma, which is apparently a reflection of the morphofunctional state of the thyroid during the period of weightlessness.

The use of artificial gravity eliminated the changes induced by weightlessness, since the number of C cells, the volume of their nuclei and degree of granulation of cytoplasm, as well as general structure of the gland itself, virtually failed to differ from the findings on rats in the vivarium control. The subsequent dynamics of increase in number and volume of C cell nuclei, particularly marked 48 h after the flight, lead us to evaluate this as an expression of an adaptive reaction directed toward increasing the release of thyrocalcitonin to stabilize calcium of bone tissue when the animals returned to earth's gravity, i.e., as an immediate reaction to gravitational stress. This thesis is also confirmed by the calcium retention found in animals flown aboard the biosatellites, which was at a maximum on the 2d-5th and 11th-12th days of the readaptation period [20].

Thus, the submitted material indicates the following: 1) absence of gravity during a long space flight leads to a decrease in functional activity of thyroid C cells in rats; on this basis, it may be assumed that, in weightlessness, C cells "do not hinder" free release of calcium ions from bone tissue; 2) exposure of animals aboard the biosatellite to artificial gravity helps preserve the morphological and functional distinctions of C cells and the thyroid itself, which are inherent in ground-based conditions; the latter warrants the belief that artificial gravity, which simulates earth's gravity, prevents changes in the thyroid that are related to weightlessness; 3) intensification of functional activity of C cells in the postflight period is a reaction to the transition from weightlessness to earth's gravity. This reaction develops in time, and it is directed toward stabilizing calcium in osseous tissue.

BIBLIOGRAPHY

1. Briskin, A. I.; Odinokova, V. A.; Kondalenko, V. F.; et al. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 2, 1971, pp 111-113.

2. Briskin, A. I.; Volozhin, A. I.; and Shashkov, V. S. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1976, pp 17-22.

3. Hirsh, O. F., and Munson, P. L. PHYSIOL. REV., Vol 49, 1969, pp 548-622.

4. Baylink, D.; Morey, E.; and Rich, C. ENDOCRINOLOGY, Vol 84, 1969, pp 261-269.

5. Kameda, J. ARCH. HISTOL. JAP., Vol 32, 1970, pp 179-192.

6. Lietz, H. VIRCHOW'S ARCH., Abt. A: "Path. Anat.," Vol 350, 1970, pp 136-149.

7. Stachura, J., and Pearse, A. G. Ibid, Pt. B: "Zellpath.," Vol 5, 1970, pp 173-186.

8. Mietkiwski, K.; Lukaszyk, A.; and Zabel, M. ENDOKR. POL., Vol 24, 1973, pp 57-70.

9. Plakhuta-Plakutina, G. I. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy" [Summaries of Papers Delivered at 10th Symposium on Space Biology and Medicine], Moscow, 1977, pp 53-54.

10. Il'in, Ye. A.; Korol'kov, V. I.; Kotovskaya, A. R.; et al. KOSMICHESKAYA BIOL,, No 6, 1979, pp 18-22.

11. Marais, A., and LaHam, V. N. CANAD. J. BIOCHEM., Vol 40, 1962, pp 227-238.

12. Grandi, P. VIRCHOW'S ARCH., Pt. B: "Zellpath., Vol 6, 1970, pp 137-150.

13. Fischer, J., and Inke, G. ACTA MORPH. ACAD. SCI. HUNG., Vol 7, 1956, pp 141-165.

14. Khesin, Ya. Ye. "Size of Nuclei and Functional State of Cells," Moscow, 1967, pp 10-33.

15. Khomullo, G. V. (editor) "Thyrocalcitonin and Repair Regeneration of Tissues Under Experimental and Clinical Conditions," Moscow, 1974.

16. Prokhonchukov, A. A.; Khomullo, G. V.; Briskin, A. I.; et al. PROBL. ENDOKRINOL. [Problems of Endocrinology], No 6, 1974, pp 80-85.

17. Matsuzawa, T., and Kurosumi, K. NAT[illegible] 213, 1967, pp 927-928.

18. Hachmeister, U.; Bonicke, J.; Lenke, M.; [illegible] al. in "Testosterone. Struma," Berlin, 1968, pp 268-271.

19. Zabel, M., and Peil, J. in "Annual of Morphology and Microscopic Anatomy," Leipzig, Pt 1, Vol 120, No 6, 1974, pp 854-861.

20. Ilyushko, N. A., and Kondrat'yev, Yu. I. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy," Moscow, 1977, p 28.

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SOME ASPECTS OF APPLICATION OF THE SYSTEMIC APPROACH TO AVIATION ENGINEERING PSYCHOLOGY

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[Article by V. A. Ponomarenko and N. D. Zavalova, submitted 26 Mar 79]

[English abstract from source]

The paper shows the role of study and analysis of systemic properties of the equipment of cockpits for its optimization. The paper describes and classifies pilot's errors caused by disadvantages of the total systemic quality of various components of the equipment. The paper presents methods for eliminating causes of some erroneous actions of pilots.

[Text] The pilot-aircraft system was the subject of studies in human engineering in aviation. The properties of a system cannot be reduced to the sum of properties of its elements, since the latter interact with one another and their properties emerge in their correlations [1]. As applied to the pilot-aircraft system, this is manifested by the fact that the efficiency and reliability of the system is not determined by biological and psychological traits of the pilot considered separately or by the technical properties of equipment, but by the aggregate of properties of interaction between man and machine, which are demonstrable only in the process of control, when man uses machines.

The components of a system have a systemic [integral] quality, in addition to their inherent natural ones. A systemic quality refers to the property of a system component that is expressed through the integrative properties of the aggregate and integrity of the system [1]. For example, the reliability of actions is the systemic quality of the pilot as a component of the pilot-aircraft system, which can be demonstrated only when the pilot interacts with the aircraft.

Aviation psychology deals with a complex system, which includes as components both man and machine. Efforts to study the features of a pilot (his skills, ability, attention, memory, thinking, etc.) and

technical characteristics (controllability and stability of the aircraft, information model, etc.) separately and then add up the obtained data failed to yield the desired result, i.e., to evaluation of tension and difficulty of pilot work, reliability and efficiency of his actions under different flying conditions. This occurs because separate studies of components do not and cannot make it possible to characterize systemic qualities.

We shall discuss the distinctions of a systemic quality on the example of evaluation of the quality of an ejection seat. If the latter is only considered as an ejection device, rating of its quality would be wrong, since the seat should provide for convenient manual and foot control, accessibility of all aircraft controls, possibility of adjusting seat height, as well as serve as a means of survival after ejection, i.e., in the pilot-aircraft system the rating of the seat should be different from a rating thereof solely as an ejection device. It would seem that this is a fact, yet in designing different types of cockpit equipment the multifunctionality of each component, its intrasystemic relations and dependence of quality on how the equipment will be used in the work process are often overlooked.

The use of the systemic approach is particularly important for solving the problem of flight safety. We shall deal with interaction between two components of the pilot-aircraft system: technical and psychological (human). The requirement of the technical component of the system is primarily that the aircraft equipment conform with the capabilities and properties of the man who controls the aircraft, or the quality of adjustment [fitting together] of the equipment to the pilot. In order to design an aircraft with the quality of fitting together, one must conduct scientific research directed toward assuring reliability of equipment, laboratory and bench tests for structural strength of the aircraft, flight tests of soundness and controllability of the aircraft in different flight conditions. Human engineering studies of the quality of interaction between the pilot and aircraft, including situations where there are malfunctions (studies of reliability of back-up equipment provided by man) are also important. It is expressly the adjustment of equipment to the pilot's properties that is a systemic quality of the technical component that aids in reliability of the pilot's provisions for malfunctioning equipment and, consequently, flight safety. The systemic quality of the psychological component is the efficiency and reliability of actions by the pilot controlling the aircraft. This systemic quality is obtained by means of special training for operation of specific equipment, for action in case of technical malfunction, purposefulness of the pilot with regard to performing the tasks, for which the pilot-aircraft system is designed, and, of course, adjustment of equipment to man.

The systemic qualities of the technical and human components--adjustment of equipment to man, efficiency and reliability of man's action--do not

exist apart from one another and cannot be manifested outside the pilot-aircraft system. Of course, providing for safety cannot be achieved only by strengthening the technical component (refining instruments, automating control, etc.) without consideration of human properties or, on the contrary, only the human component (development of skills, life support, screening, setting labor standards, etc.) without consideration of the quality of aircraft equipment. The systemic approach to solving the safety problem is based on determination of correlations and interrelations between these two components.

Thus, the pilot and aircraft are united in a system which, like any system, consists of an aggregate of components that are coordinated to reach a common goal. The efficiency of the system is not so much a function of the components proper as of their interactions and interdependence. This means that neither a trained specialist nor refined equipment considered separately can guarantee the safety of a flight.

The cause of flight accidents is often related to human errors. In this regard, we shall discuss the possibility of using the systemic approach to the study of pilot errors. Heretofore, only the personal factor, i.e., psychological, physiological and other traits inherent in man as a concrete individual, was often mentioned in establishing that human error was the cause of a flight accident. We believe that use of the concept of "personal factor" is not sufficient to refer to pilot error as a cause. When reference is made to the personal factor, the process of interaction between man and equipment is disregarded, and without this it is impossible to establish the true cause of a flight accident [or incident]. The systemic approach to analysis of causes and errors made it necessary to introduce another concept, "the human factor,"* which contains the idea of dependence of characteristics of human actions on the properties of equipment. In this case, pilot error is an integral indicator of the shortcomings of interaction between man and equipment, adjustment of equipment to man.

The systemic approach made it possible to disclose a class of errors "built into equipment," embodied in it due to underestimation of human traits in designing it. These errors are not referable to man alone, they are manifested through interaction between the pilot and aircraft. The lack of a systemic approach to analysis of the causes of errors results in classification of errors built into equipment, when they are manifested, as errors of action by the fault of man. For example, there is the error of moving a control too far, which causes impairment of piloting conditions. This error is typical of control systems that are so designed that, in the event of increased acceleration [or overload],

*The concept of "human factor" is in the realm of engineering psychology. However, in recent years, the words "personal factor" and "human factor" have been used as synonyms in investigations of flight accidents.

the pilot would reduce the muscular force applied to alter this. Such a control system requires fine differentiation between muscular exertions by the pilot in the presence of high accelerations, i.e., expressly under conditions when such differentiation is impossible. In this case, the condition is built into the equipment that provokes pilot error. In its design, due consideration was not given to the fact that the very presence of acceleration impairs subjective evaluation of the muscular force applied to the controls, and it is perceived as weaker.

The systemic approach makes it possible to choose steps that aid in overcoming pilot error. It is directed toward demonstration of the genesis of erroneous action. For this purpose, one must examine integral activity. According to psychological theory [2], the activity meets certain demands of man and is characterized by a certain motive. Activity is performed through actions that are directed toward a concrete result and determined by consciously set goals. The action is performed through different operations, the composition of which is not related to the goal, but to the conditions under which the goal must be reached. Thus, a distinction is made between three levels in the macrostructure of activity: activity, action, operation.

An error may occur on each macrostructural level of activity. An error occurs on the first level as a result of distortion of the motive, the need of the man performing the activity. On the second level, it could result from inconsistency bewtween man's subjective goal and the objectively set task, the result of distortion of the conceptual model (image-goal) and paucity of operational images. On the third level, the error is related to inconsistency of conditions and tasks, and it is manifested by failure to perform certain movements, poor coordination, missing a signal, etc. While prevention of errors due to motivational flaws (first level) involves training of the pilot's personality, screening of individuals for flight work, to overcome errors of action requires consistency of the information model with the pilots need for information and training, an information model that would be adequate to the pilot's tasks. Overcoming errors on the third level requires the development of automated skills, optimization of arrangement of controls and indicator devices in the cabin, better design of the dials of the indicator devices.

Apparently, a distinction is made between internal mechanisms that are similar in manifestation of error and, consequently, the measures to overcome these errors, depending on the genesis of the error. Consideration of the cause of motor or other errors only as a deficiency referable to skill is tantamount to canceling them out, reducing them to the operational level (occurring on the third level). As a result, the impression is gained that it is very simple to eliminate the cause of errors. The corresponding measures are developed; however, they turn out to be ineffective. Use of the systemic approach, which implies understanding of pilot activity, which is not reduced to the sum of

operations, indicates the complexity and multivalence of causes of errors. First of all, it takes into consideration the relation of the error to the goal of action, to characteristics of the image that regulates action. Only the systemic approach permits disclosure of the deep internal causes of pilot error. Systemic analysis shows that the origin of errors cannot be deduced from one source and reduced to one cause. Each specific error is caused by a multitude of causes.

Let us consider how different sources and causes of errors are interrelated in a pilot-aircraft system. Man, who has certain personality, professional and somatic distinctions, and equipment, which includes the features of the pilot's work place, information model, control systems and aircraft aerodynamics, are the chief cuases of errors. Under actual flight conditions, the sources of errors are interrelated. There are two initial causes of errors: flaws referable to interaction between man and machine (human factor) and limited capabilities and shortcomings of the pilot (personal factor). The immediate causes of errors related to the human factor are incomplete, false and vague information, uncoordinated delivery of signals, poor design of indicator dials, low attention-attracting effect of signaling devices, inconvenient location of control levers, inconsistency of laws for control and human reactions, uncoordinated distribution of functions between man and automatic equipment, and many others. The immediate causes of errors related to the personal factor may be poor pilot training, inadequate motivation, unfavorable individual psychological distinctions, health-related flaws, etc. Errors, the cause of which are flaws in interaction between the pilot and aircraft, are aggravated under the influence of adverse flight factors, as well as an adverse personal factor. Favorable personality traits in the pilot, on the contrary, help avert part of the consistent errors built into the equipment or minimize their adverse consequences.

The material we have discussed helped demonstrate the complexity of such an ordinary factor, it would seem at first glance, as pilot error. Systemic analysis demonstrated the elements of its complexity: an error occurs due to flaws in the aggregate systemic quality of some component of the system, and its cause cannot be disclosed without consideration of the relations between components in the pilot-aircraft system.

Use of the systemic approach to the study of flight work makes it possible to derive some conclusions of practical importance: 1) psychological forecast of flight safety should be made on the basis of studying the integral pilot-aircraft system, studies of the characteristics of interaction between pilot and machine under different flying conditions; 2) improvement of efficiency and reliability of flight work should be made by providing for the systemic quality of the technical component, i.e., adjustment of equipment to man; 3) most often, pilot error is not related exclusively to the personal factor; for this reason, unilateral orientation of efforts toward education, training and medical supervision cannot assure a substantial decline in number of in-flight

errors. To prevent errors, it is imperative to make a concrete analysis of all elements of interaction between the pilot and aircraft equipment, in order to prepare recommendations for directed training of flight personnel and planning pilot activity in the aspect of human engineering.

BIBLIOGRAPHY

1. Kyaz'min, V. P. VOPR. FILOSOFII [Problems of Philosophy], No 9, 1976, pp 81-94; No 10, pp 95-106.

2. Leont'yev, A. N. "Activity. Consciousness. Personality," Moscow, 1975.

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EFFECT OF PROLONGED +Gz ACCELERATIONS ON HUMAN PERFORMANCE

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[Article by A. S. Barer, T. A. Sokolova, V. M. Tardov and Yu. P. Yashin submitted 26 Jul 79

[English abstract from source]

With an increase in acceleration value the accuracy of human performance decreases. This becomes very noticeable at $+G_z > 5$ g. In this situation work capacity can be raised by increasing an angle between the G_z vector and the long axis of the human body. Pilots need to be tested for acceleration tolerance before they are allowed to fly at $+G_z \geq 8$ g.

[Text] It is known that the extent of circulatory disturbance under the influence of acceleration (other conditions being equal) is determined by the magnitude of its component in the axis of the pilot's head--pelvis ($+G_{z1}$), which is related both to the magnitude of overall acceleration of the aircraft and the angle between the direction of its action and longitudinal body axis [1-4]. Obviously, as this angle increases, the height of the hydrostatic column of blood between the heart and peripheral blood vessels diminishes. As a result, there is less deposition of blood, improved venous return to the heart and delivery of blood to the brain which, in turn, leads to better human performance [fitness]

This means of improving fitness i the presence of accelerations has found wide use in the design of manned spacecraft, and it is beginning to be adopted in the aircraft industry [5, 6]. In this regard, reports have recently appeared in the press concerning the results of research on the performance of human operators under different conditions, and for this purpose diverse flight simulating devices were used, in particular centrifuges [5-13]. At the same time, the influence of high $+G_z$ inherent in aviation on specific operator activity of pilots has not yet been sufficiently studied.

We report here the results of a study of the effects of +Gz acceleration and relative increase in angle of its orientation in relation to the longitudinal axis of the body on pilot performance.

Methods

There were 13 men ranging in age from 22 to 39 years participating in the studies; they were deemed fit for flight work with regard to their physical condition and had undergone a complete course of training on "piloting." This study was conducted on a piloting complex, which included a centrifuge with 8-m arm and a computer (Figure 1).

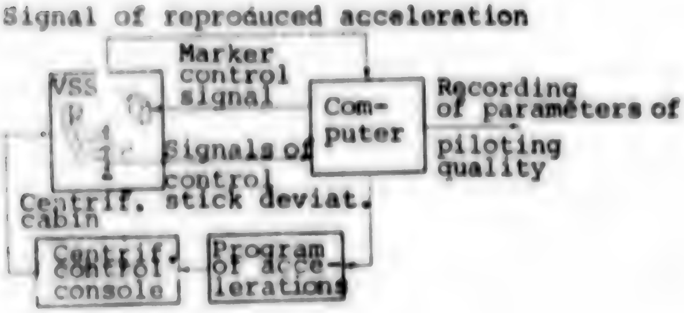


Figure 1. Diagram of flight simulating complex

To evaluate operator performance, the test consisted of the task of tracking a moving marker light projected on the screen of a visual situation simulator (VSS). Deviations of the marker were compensated by means of a control stick [handle]. Signals proportionate to movement of the stick were transmitted from the centrifuge cabin to the computer, which solved equations of motion and controlled movement of the marker over the VSS screen to correspond to the task of piloting an aircraft.

The studies were conducted using different levels of accelerations at angles of 23 and 35° to the longitudinal axis of the human body, which enabled us to test performance as related both to the magnitude and direction of acceleration. The results were expressed in the form of parameters as functions of magnitude of the longitudinal component of acceleration, $+G_{zl}$, chosen as the general parameter for this series of studies.

In all, we conducted 207 tests with accelerations of 2, 4, 5, 6, 8 and 9 units.

Quality of performance was rated according to the mean square error of tracking σ. To evaluate distribution and range of attention, the subject

checked the quality of his own performance: at times when in his opinion piloting accuracy was within the specified range he depressed a button. We took into consideration the number N of correct ratings of accuracy. In addition, to assess performance we also determined the maximum possible "piloting" time during exposure to 9 unit acceleration.

In all of the tests, we recorded the acceleration, EKG, systolic arterial pressure (AP) in vessels of the concha, photoplethysmogram (PPG) of the same region, minute volume of respiration (MV) reduced to the unified standard in the BTPS system.

In all cases, an anti-G suit was worn. In addition, to increase endurance of accelerations, we created tension of prelum abdominale and lower limb muscles.

The digital data obtained in the experiments were submitted to statistical processing using the system adopted in biomedical research.

Results and Discussion

These studies revealed that accelerations have a substantial effect on performance. Figure 2a illustrates the relative tracking error and relative decrease in number of correct self-evaluations of performance quality as a function of magnitude of the longitudinal component of acceleration G_{z1}. As can be seen in this figure, this dependence is particularly marked with accelerations in excess of 5 units, and there was the same degree of build-up in tracking errors and decrease in correct subjective rating of piloting quality up to $+G_{z1} \leq 7.5$ units. At higher acceleration levels, the number of correct subjecting ratings decreased much more than the increase in tracking error. Evidently, this phenomenon is related to the fact that the scope of operator attention under such conditions is virtually depleted, and he is unable to reliably perform any operation other than the main one (for example, "piloting").

The change in quality of "piloting" was quite consistent with the tested physiological parameters. Processing of physiological parameters and analysis of the subjects ratings enabled us to systematize the factors that limited endurance of accelerations and performance. The most frequent signs leading to loss of control or determining the range of endurance were found to be visual disorders, general fatigue and pain in the upper third of the forearm (ulnar surface), elbow and distal region of the arm.

As we know, visual disorders during exposure to accelerations are due to poorer circulation in the retina. We demonstrated a correlation between mean and lowest systolic AP in the "plateau"* in the region of the head

*"Plateau" refers to the period of centrifuge rotation with a constant level of acceleration.

(sensor on the ear lobe), as well as amplitude of ear pulse, and the $+G_{z1}$ component of acceleration (Figure 2, b, c). As can be seen in this figure, the mean AP and ear pulse amplitude begin to decline appreciably with $+G_{z1}>4.5$ units. The minimum AP and ear pulse amplitude begin to decline at lower acceleration levels, and with $+G_{z1} = 6.5$ units they reach 30 mm Hg and 30% of initial amplitude, respectively, which is indicative of the possibility of visual disorders [14, 15].

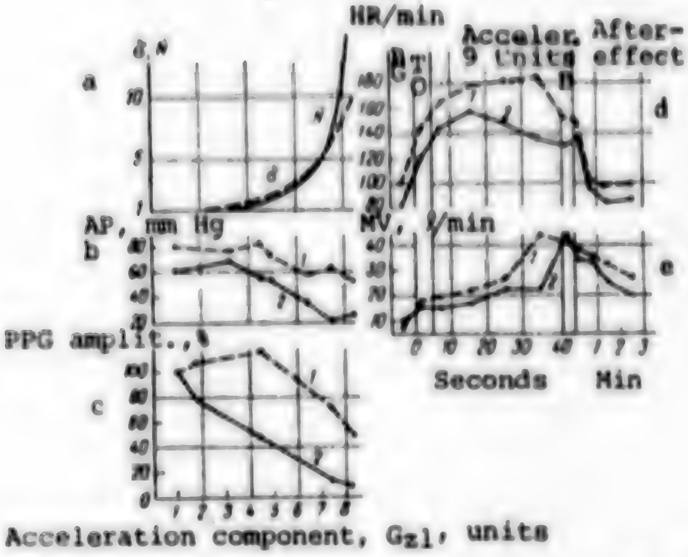


Figure 2. Changes in performance and some physiological parameters (statistical means) under the influence of different levels of acceleration

Key:

a) tracking error as related to base value ($\overline{\sigma} = \frac{\sigma \text{ with accelerations}}{\sigma \text{ in the initial state}}$), and degree of decrease in number N of correct subjective assessment of performance ($\overline{N} = \frac{N \text{ in the initial state}}{N \text{ with accelerations}}$)

b) mean (1) and minimum (2) systolic AP on "plateau"

c) mean (1) and minimum (2) amplitude of ear pulse on "plateau" (% of base values)

d,e) heart rate (HR) and MV in subjects with stable (1) and vagal (2) types of chronotropic cardiac reaction to 9-unit acceleration directed at an angle of 35° to the longitudinal axis of the body

BG) background

TO) take-off acceleration

B) braking

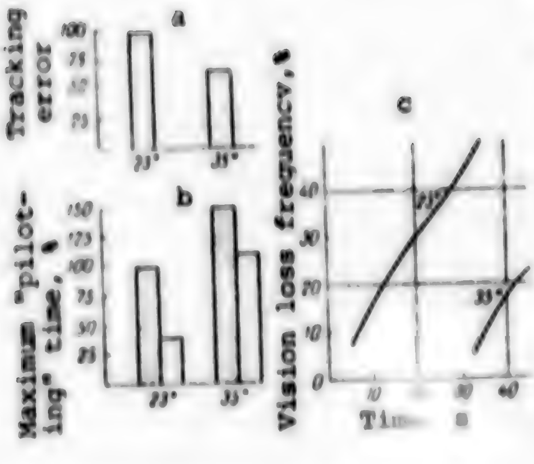


Figure 3.
Comparative evaluation of performance parameters (statistical means) with 9-unit acceleration at angles of 23 and 35° to longitudinal axis of the body

a) relative tracking error
b) correlation between maximum "piloting" times (striped columns, time for all subjects; white, for the group less tolerant to accelerations)
c) frequency of loss of vision (% of total number of tests) as a function of time

Fatigue, as a factor limiting performance with exposure to accelerations, is determined by the limited "energy resources" for compensation of functions and different systems of the body and maintenance of high muscular tension.

As for the pain in the arms with accelerations of the order of $+G_{z1} = 8.0 \div 8.5$ units, they can be attributed to elevation of hydrostatic pressure and increased delivery of blood to vessels of the areas involved.

Very typical changes were observed under the influence of accelerations in dynamics of heart rate (HR) and pulmonary ventilation. Thus, starting at about the 15th s of accelerations of 9 units, there was distinct demonstration of two types of chronotropic cardiac reaction, stable and vagal [16], and they corresponded to different dynamics of changes in MV (Figure 2d). It is important to note that appearance of relative bradycardia was not associated with either decreased endurance or diminished performance.

This study also revealed that, among individuals who had undergone medical examination for determination of fitness for flying with positive results, there was rather clear distinction of a group of subjects with relatively poorer endurance of accelerations. Thus for the less resistant group of subjects, maximum piloting time at $+G_{z1} = 8.3$ units was one-fourth the time for the others. The latter circumstance convinces us of the desirability of examining pilots for endurance and performance at Gz accelerations, and this is consistent with the recommendations of a number of other researchers [12, 17].

The results revealed that maximum "piloting time" at 9 units of acceleration increases (by a mean of 1.5 times) while tracking error decreases (to the same extent) when the angle between the vector of acceleration and

longitudinal axis of the human body is increased from 23 to 35° (Figure 3, a, b). And for the group of less tolerant subjects, the increase in maximum "piloting" time is even greater (by 3 times; see Figure 3b).

Finally, it is important to mention that an increase in angle of tilt of the seat provides better compensation of circulation in the region of the head and, consequently, lowers appreciably the frequency and severity of visual disorders that limit the time of retention of fitness for work (Figure 3c).

BIBLIOGRAPHY

1. Barer, A. S.; Golov, G. A.; Zubavin, V. B.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow, Coll 1, 1967, pp 30-42.

2. Gell, C. F., and Hunter, N. N. J. AVIAT. MED., Vol 25, 1954, pp 568-577.

3. Kotovskaya, A. R.; Vasil'yev, P. V.; Lapin, B. A.; et al. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 4, 1965, pp 322-332.

4. Sergeyev, A. A. "Physiological Mechanisms of Effects of Accelerations," Leningrad, 1967.

5. Burton, R. R.; Japietro, P. F.; and Leverett, S. D. AVIAT. SPACE ENVIRONM. MED., Vol 46, 1975, pp 887-897.

6. "Special Report F-16 Multinational Fighter Program," AVIAT. WEEK SPACE TECHNOL., Vol 106, No 18, 1977, pp 44-130.

7. Prilliman, F. W. Nuff, W. W., Jr.; and Hooks, J. T., Jr. J. AIRCRAFT, Vol 6, 1969, pp 353-359.

8. Acklat, D. J. AIRCRAFT ENG., Vol 44, 1972, pp 4-8.

9. Volkov, A. A.: Denisov, V. G.; Kirilenko, Yu. I.; et al. in "Sistema 'Chelovek i avtomat'" [Man-Machine Systems], Moscow, 1965, pp 215-228.

10. Kakurin, L. I.; Kotovskaya, A. R.; Filosofov, V. K.; et al. Ibid, pp 241-244.

11. Zorile, V. I., and Kupriyanov, A. A. VOYEN.-MED. ZH. [Military Medical Journal], No 6, 1972, pp 89-94.

12. Barer, A. S.; Yeliseyev, A. S.; Panfilov, V. Ye.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1968, pp 54-57.

13. Kotovskaya, A. R.; Vartbaronov, R. A.; and Khomenko, M. N. Ibid, No 6, 1977, pp 12-19.

14. Kotovskaya, A. R.: Vartbaronov, R. A.; and Nikol'skiy, L. N. Ibid, No 1, 1975, pp 58-66.

15. Suvorov, P. M.; Babushkin, V. I.; and Arkhangel'skiy, D. Yu. Ibid, No 3, 1976, pp 64-67.

16. Tikhomirov, Ye. P. Ibid, No 3, 1969, pp 71-75.

17. Suvorov, P. M. "Physiological Tests on Centrifuges in Medical Certification of Fitness for Flying and the Screening System," author abstract of doctoral dissertation, Moscow, 1969.

UDC: 612.843.312-06:612.745.1].014.47:531.15

HUMAN COLOR DISCRIMINATING FUNCTION WITH MUSCULAR TENSION DURING EXPOSURE TO VESTIBULAR STIMULI

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 41-44

[Article by Zh. M. Kudryashova and A. A. Shipov, submitted 10 May 79]

[English abstract from source]

Human studies have demonstrated that arbitrary tension of muscles (back and legs) during repeated vestibular exposures not only delays the development of motion sickness but also contributes to the maintenance of color discriminative stability of the visual function.

[Text] The safety of movement over all transport routes, including space flight routes, depends largely on the state of the operator's color vision. Yet the color discriminating function of the eyes of an individual performing operator work under specific conditions of exposure to unusual vestibular stimuli inherent in moving systems has not been studied at all.

In this work we tested color-discriminating function of the human eyes under conditions that are often encountered when operating ground and air types of transport, namely during tension of muscles of the shoulder girdle and legs during exposure to recurrent vestibular stimuli.

Methods

We conducted these studies on 50 individuals of both sexes ranging in age from 20 to 35 years.

Vestibular stimuli were simulated by the system of I. I. Bryanov [1]. The body was inclined and straightened during rotations with maximum concurrent tension of muscle groups of the shoulder girdle and legs. In all, there were 15 rounds of rotation. The test was stopped if grade II

vestibulovegetative reactions (VVR-II--pallor, nausea, retching, hyperhidrosis) appeared during rotation.

As an objective record of autonomic reactions before and immediately after the vestibular test, we determined the heart rate (HR) according to the R-R interval on the EKG, maximum and minimum arterial pressure (APmin and APmax) according to N. S. Korotkov, caliber of central retinal veins and arteries (CCRV and CCRA) using a PEO-58 scope ["visuscope"], and pressure in the central retinal artery (PCRA) using an ophthalmodynamometer of the Krasnogvardeyets plant.

Color visi[illegible] [illegible]as evaluated on the basis of level of functional stability of color d[illegible]imination, spectral and color contrast sensitivity [2]. Color con[illegible]t sensitivity was tested in the long- (red, 665 nm), medium- (green, 5[illegible]m) and short-wave (blue, 465 nm) bands of the visible spectrum. Spectral sensitivity was tested in the ranges of 665-655, 530-520 and 475-465 nm by determining the number of thresholds. Functional stability of color discrimination was studied by determination of time thresholds of adisparopia (ADP) with presentation of red-gray and blue-gray equations. Illumination of the test tables constituted 70-80 lx on white.

ADP was examined before rotations, in the intervals between them up through the 8th round, after the 10th and 15th rounds, as well as in the 5th, 10th and 15th min of the aftereffect period. Spectral and color contrast sensitivity was determined before, immediately after and 15 min after rotation. Background tests were made after adaptation for 10 min to white light, with mean spherical illumination in the room of 35-40 lx. The tests were made during the same time of year and day.

Muscular tension was not produced in the control studies.

Studies were also conducted with tension of muscles with the trunk tilted and straight, but without rotations.

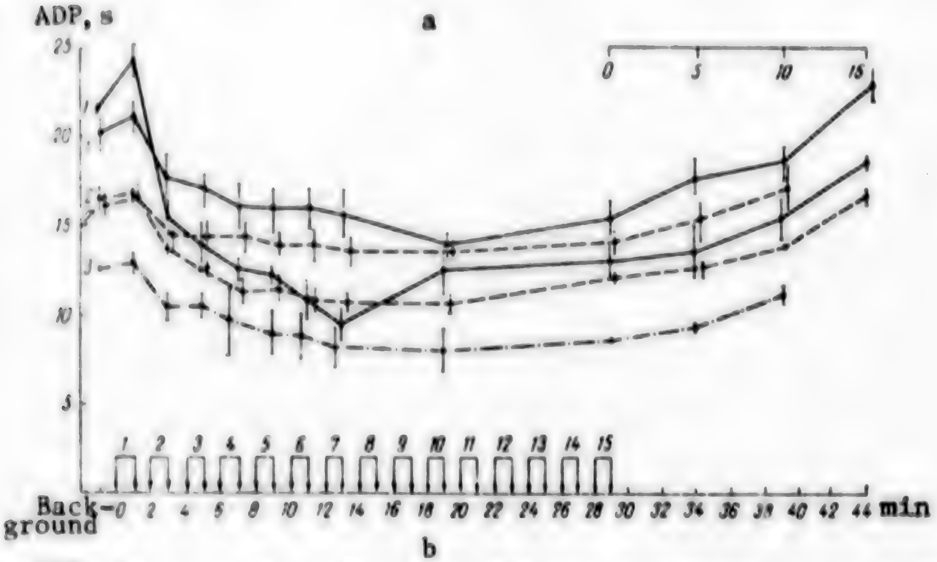
On the basis of analysis of the findings on subjects who failed to present clinically demonstrable vegetative reactions after 15 rounds of rotation, they were referred to the group with vestibular stability. Individuals who developed VVR-II in the course of control rotations made up the group with vestibular instability.

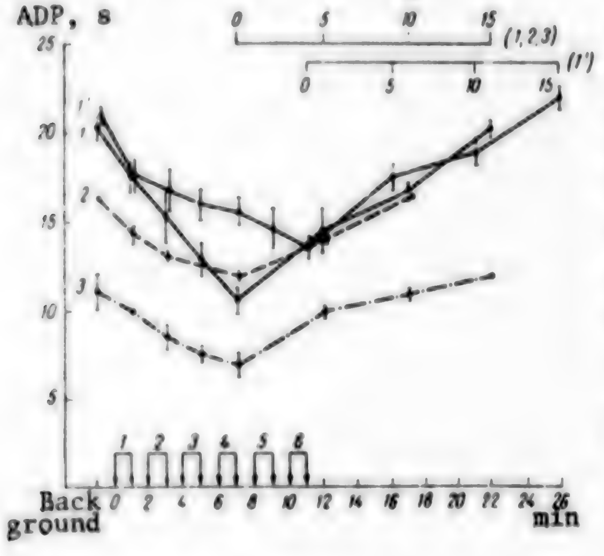
Our studies also made it possible to assess the effect of voluntary muscular tension on human vestibulovegetative stability.

The experimental data obtained were submitted to statistical processing, using the criterion of Student ($P<0.05$).

Results and Discussion

The change in ADP thresholds for different colors in both groups of subjects in the control series of studies (without muscular tension) is illustrated in the Figure and was described in detail by us previously [2].





Changes in ADP thresholds for different colors during vestibular stimulation in subjects with (a) and without (b) vestibular stability. X-axis, time (min). The numbers over the arrows refer to sequential round of rotation. Top horizontal scales, rotation aftereffect time (min)

1, 2) for red and blue, respectively
1', 2') with concurrent tension of shoulder girdle and leg muscles
3) for blue

The rate of decline of thresholds of color discrimination during muscular tension was substantially slower in the red and green bands of the spectrum in "vestibulostable" subjects (12 people), as compared to the control tests, while only a mild tendency toward slowing was noted in the blue band (see Figure, a). In the group with vestibular instability (38 people) there was also a decline in rate of decrease in thresholds for red (see Figure, b). In the blue-green part of the spectrum, no reliable differences from the findings in control tests were demonstrated.

Without rotations, bends with muscular tension (and without it) failed to elicit changes in color discrimination.

As can be seen in the Table, in stable individuals muscular tension did not alter the recorded autonomic reactions, as compared to those found in the control series of tests. At the same time, in individuals with vestibular instability, muscular tension neutralized the effects of vestibular stimulation according to virtually all parameters of peripheral and retinal circulation. They developed VVR-II only after the 6th round of rotation, rather than the 4th, as was recorded in the control series of tests (see Figure, b).

Parameters of peripheral and retinal circulation after exposure to vestibular stimuli

Test conditions	Group	PCRA, mm Hg	CCRV, µm	CCRA, µm	HR/min	APmin, mm Hg	APmax, mm Hg
Background	Vestibular stability	39±0.61	150±1.9	86±2.1	73.8±3.1	77.0±2.9	113.0±4.1
	Vestibular instability	39±0.87	146±2.1	83±1.8	74.5±2.5	78.0±2.1	115.0±1.84
Without muscle tension	Vestibular stability	44±2.4	150±1.8	80±1.9	71.5±2.5	75±2.1	110.4±3.8
	Vestibular instability	45±0.62	156±3.1	79±0.81	71.4+2.1	79.6+2.1	125±2.1
With muscle tension	Vestibular stability	40±0.7	150±1.8	82±2.3	78±1.5	80±1.7	110±2.3
	Vestibular instability	41±1.4	150+2.9	80±1.5	73±3.2	ɔ5.0±3.1	118.0±4.1

Thresholds of color and brightness contrast sensitivity did not change in either group, as in the control series of tests.

It is known that there is attenuation of many physiological reactions with static muscular tension. For example, there is depression of such a strong unconditioned reflex as retching after administration of apomorphine [3]. Static musuclar tension of the elevated arms with a weight eliminates the autonomic effect of vestibular stimuli, manifested by constriction of cutaneous vessels [4]. Voluntary tension of back muscles, as well as those of the legs, during exposure to vestibular stimuli analogous to those we used attenuated the autonomic symptoms of motion sickness [5].

The beneficial effect we demonstrated on voluntary muscular tension on vegetovestibular stability and chromatic vision with exposure to vestibular stimuli is apparently mediated by the cerebral cortex. Indeed, as has been comprehensively substantiated in [2], the decline of ADP thresholds for all colors, observed with repeated exposure to vestibular stimuli with relaxed muscles, is indicative of developing visual and general fatigue, and it is an indication of inhibitory processes in the visual cortex. The function of photoreceptors remains unaffected, since spectral and contrast color sensitivity, which characterize primarily the condition of the retina, remains virtually unchanged in both groups of subjects. A circumscribed focus of excitation appears in the motor cortex with voluntary tension of muscles, and it is sustained by formation of volitional impulses, on the one hand, and afferentation from proprioceptors and chemoreceptors of functioning muscles, on the other [6]. Brief muscular tension apparently creates favorable conditions for irradiation of excitation over the cortex, which delays development of inhibitory processes with repeated vestibular stimulation. In our opinion, for expressly this reason there is slower decline in level of stability of color vision. The inhibitory [7] function of the cortex, with reference to vegetovestibular reflexes, also remains more intact, for which reason there is delayed development of motion sickness.

Thus, voluntary tension of muscles (of the back and legs) during exposure to vestibular stimuli not only delays development of motion sickness, but attenuates the decline in level of color discriminating stability of vision.

BIBLIOGRAPHY

1. Bryanov, I. I. VOYEN.-MED. ZH. [Military Medical Journal], No 11, 1963, pp 54-56.

2. Kudryashova, Zh. M., and Shipov, A. A. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1979, pp 25-31.

3. Sukhanov, A. A. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 1, 1958, pp 14-18.

4. Rachkov, V. A. in "Motorno-vistseral'nyye is vistsero-motornyye refleksy" [Motovisceral and Visceromotor Reflexes], edited by M. R. Mogendovich, Perm', 1963, pp 203-213.

5. Ayzikov, G. S.; Yemel'yanov, M. D.; and Ovechkin, V. G. KOSMICHESKAYA BIOL., No 3, 1975, pp 68-74.

6. Vereshchagin, N. K. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 7, 1957, pp 699-704.

7. Khilov, K. L. "Function of Equilibrium Organ, and Motion Sickness," Leningrad, 1969.

UDC: 612.748.014.477

EFFECT OF TRANSVERSE ACCELERATIONS ON INNERVATION OF THE GUINEA PIG'S CRURAL SKELETAL MUSCLES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 44-48

[Article by V. Ya. Osaulenko, submitted 20 Dec 78]

[English abstract from source]

Guinea pigs were exposed to chest-to-back acceleration of 8 G for an hour. This exposure brought about significant morphological changes of a primary-reactive pattern in nerve elements of skeletal leg muscles. With time they enhanced. 6 hours and then 3 days after the experiment a small portion (1—1.5 %) of nerve fibers underwent fragmentation and degradation. Motor nerve endings showed the highest resistance. The first signs of restitution of changes in the peripheral nervous system were seen 6 days after the exposure. Nerve fibers did not return to the normal 9 days after the beginning of the experiment.

[Text] Many facts have been accumulated to date indicative of changes in the peripheral nervous system (PNS), blood vessels [1-7], atria [8-11], digestive tube [12-15], larynx [16], adrenals [17] and other internal organs under the influence of accelerations in different directions. However, there have been no studies of the effect of this same extreme factor on neural elements of skeletal muscles. In view of the foregoing, as well as the special role of the nervous system in maintaining structural integrity of muscles, our objective here was to study the state of the muscular nervous system after exposure to accelerations in the chest--back direction.

Methods

The material we studied consisted of leg muscles of 25 guinea pigs that had been exposed once to accelerations of 8 units (rotation on a centrifuge for 1 h) in the chest-back direction. During the experiment, 20% of the animals died. We collected material from them immediately after

death was established. Other animals were sacrificed and material was collected from them immediately after rotation, then 6 h, 1, 3, (and 9 days later. Leg muscles of five intact animals served as a control. The material to be examined was fixed by submersion in 12% neutral formalin. Motor nerve fibers and their endings were demonstrated by various methods of silver nitrate impregnation (Bielschowsky-Gross, Schultze, Campos and others) followed by gold stain and additional staining of sections with hemalum and eosin. The myelin sheaths of myelinated fibers were demonstrated with hematoxylin varnish according to Spielmeyer.

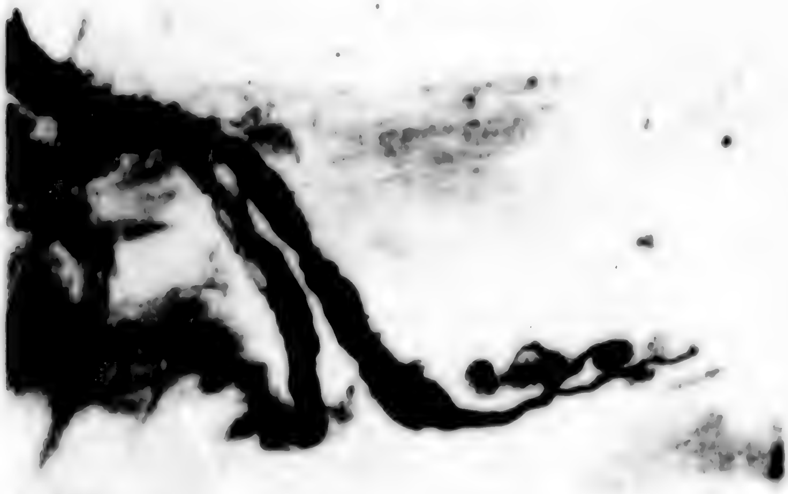


Figure 1. Reactive changes in nerve fibers (hyperimpregnation, swelling of axis cylinders and vacuolization of neuroplasm. Guina pig leg muscle after exposure to acceleration of 8 units for 1 h. Here and in Figures 2 and 3, Bielschowsky-Gross stain; microphotograph, MBI-6, ocular 7×, objective 40×

Results and Discussion

Examination of histological preparations of experimental material shows that single exposure to transverse accelerations with intensity of 8 units

for 1 h elicits significant structural changes in the nerve elements of the animals' skeletal muscles. Overt signs thereof were demonstrable immediately after terminating the experiment, at which time they were of a primary, reactive nature. The most typical manifestations of PNS changes in these animals was distortion of impregnation properties (hyperimpregnation, dyschromia) of 95-97% of the nerve fibers of large, medium and even small caliber, as well as appearance of generalized or localized swellings along the course of nerve fibers of the first two sizes, appearance of bulges on their surface in the shape of mushrooms and spines, unravelling of neurofibril bundles at the sites of axonal thickening, and formation of centrally localized vacuoles as a result of hydropic neuroplasmic disturbances (Figure 1). As a rule, such fibers also present signs of irritation of Schwann's syncytium and unusual argyrophilia. The preterminal part of the motor nerve fibers was found to be the most labile, and it presented the most severe changes. As compared to others, the axis cylinders of small-caliber nerve fibers were very resistant. The motor nerve endings were particularly resistant to accelerations. During this stage of the observation period they retained entirely their inherent structure.

Six hours after exposure, PNS of the extremital skeletal muscles presented considerable deterioration. At this time, virtually all of its nerve fibers were altered. Moreover, in this group of guinea pigs, unlike the animals referable to the preceding examination time, some nerve fibers (about 1%) were subject to destruction and presented a state of fragmentation and granular breakdown. Concurrently, there was an increase in number of axons with signs of irritation, increase by one-third in number and size of congested elements in neuroplasm of the preterminal part of the nerve fibers. The motor endings of these animals, unlike those previously described, no longer consisted of a homogeneous group. Along with the usual motor plates, at this time we already encountered isolated motor nerve elements (no more than 2%) the terminal branchings of which were very strongly impregnated with silver and appeared thicker and coarser.

There was even more marked primary reactive changes in PNS of the crural skeletal muscles 1 day after exposure. However, we failed to detect new forms of changes, but there were qualitative and quantitative ones. It should be noted that, as compared to the preceding stage, nerve fibers with signs of dyschromia were encountered more often. Neuroplasmic congestion in the preterminal parts of many axons increased by 1.5-2 times in size. Although the number of vacuoles in nerve fibers did not change, they occupied chiefly a peripheral position, which is indicative of separation of these drops of fluid and subsequent elimination from fibers. We did not observe signs of destruction of new nerve fibers in this group of animals. As for the number of motor plates that were coarse, it increased by 2 times at this time, as compared to the preceding stage, constituting about 4% of those demonstrated. The result of the motor nerve endings retained their usual structure, which is indicative of considerable resistance of most of them to the factor in question.

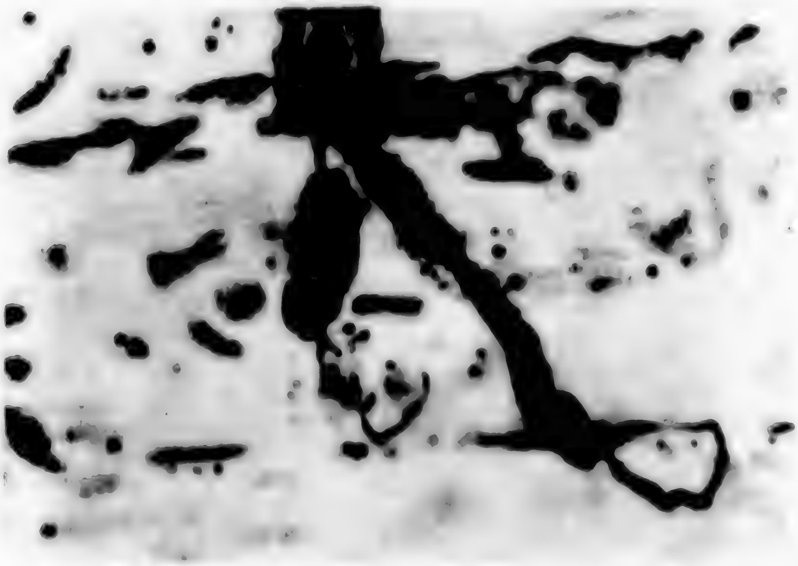


Figure 2. Formation of large accumulation of neuroplasm in preterminal part of nerve fiber; crural muscle of guinea pig 3 days after accelerations of 8 units for 1 h

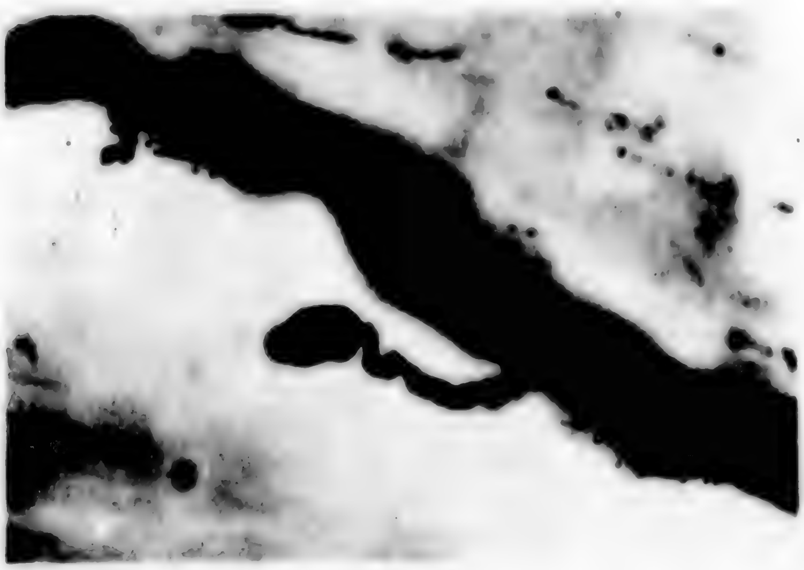


Figure 3. Neuroma in region of neuroplasmic congestion formed as a result of destruction of axonal terminal; guinea pig crural muscle 6 days after 8-unit accelerations for 1 h

Three days from the start of the experiment, there was further development of the previously described changes in the PNS of crural skeletal muscles. By this time there was enlargement of swellings of axis cylinders, mainly of thick myelinated nerve fibers. The vacuoles were encountered less often and usually situated in the superficial parts of the fiber. The neuroplasmic congestions of the preterminal part of the axons became larger, up to 40-50 μm in diameter (Figure 2). In this group of animals, we more often encountered nerve fibers in a state of degradation. The number of motor endings with signs of coarsening did not exceed 5% of the total number, even though it increased. The nerve endings of such plates appeared not only thicker than usual, but without the inherent loops, knobs or grids on the endings. The remaining 95% of the motor endings of skeletal muscles of this group of animals failed to reveal any visible changes.

Six days after exposure to accelerations, the changes in PNS of crural skeletal muscles consisted of essentially the same forms as before, but a significant part thereof showed regression. For this reason, the overall amount of changes occurring in the preceding periods diminished on the whole, and in some cases the nature thereof changed. Thus, the number of bulges on the surface of axis cylinders diminished to almost one-half, while the remaining spines and buds decreased in height; as a result the outlines of many nerve fibers were much smoother. There was a decrease in size of swellings of axis cylinders, and it is only in the preterminal part of some axons that there was occasional retention of large congestions of neuroplasma. As a result of separation of terminal elements from such fibers, they acquired the appearance of unique "neuromas," consisting of axons ending with considerable increase in diameter, to 50 μm (Figure 3). By this time, processes of elimination of products of disintegration of nerve fibers were concluded. No degradation of other nerves was observed at this time. The number of motor endings presenting signs of coarsening of terminals increased by 1-2%, as compared to the preceding stage, constituting 6-7% of those demonstrated.

After 9 days, processes of normalization of various elements of PNS of skeletal muscles were even more distinctly manifested. However, at this stage of our studies, some of the nerve fibers and their endings retained various signs of irritation (hyperimpregnation, dyschromia, small swellings, irregular outline of axis cylinders, coarse terminals in 6-7% of the motor plates, etc.).

Thus, the following conclusions can be derived on the basis of our observations: 1) single exposure to transverse (chest-back) accelerations of 8 units for 1 h continuously induces significant structural changes in the nerve elements of crural skeletal muscles, which do not disappear entirely, even after 9 days; 2) overt signs of changes in PNS of the crural skeletal muscles are demonstrable immediately after exposure to

accelerations. Thereafter (after 7 h, 1, 3 and 6 days) they progress and extend over almost all nerve fibers of large, medium and, in part, small caliber; 3) PNS elements of skeletal muscles of the leg are subject mainly to primary reactive changes under the influence of single exposure to transverse accelerations, and they are only partially destroyed; 4) the preterminal segment is the most labile part of motor fibers exposed to accelerations; 5) the axis cylinders of small-caliber nerve fibers demonstrate high resistance to accelerations; 6) motor endings, which essentially retain their inherent structure, are particularly resistant to such conditions; 7) processes of restitution of altered nerve elements are slow, and they become noticeable 1 week after exposure to accelerations.

BIBLIOGRAPHY

1. Kurkovskiy, V. P. in "Voyen.-med.akad. im. S. M. Kirova. Sbornik referatov nauch. rabot za 1953-1955 gody" [Military Medical Academy imeni S. M. Kirov: Collection of Abstracts of Scientific Papers for 1953-1955], Leningrad, 1957, pp 106-108.

2. Nikolayeva-Luneva, L. N. "Sbornik trudov Tyumen. med. in-ta" [Collection of Works of Tyumen' Medical Institute], Vol 1, 1968, pp 137-141.

3. Klebanov, V. M. "Trudy Tselinograd. med. in-ta" [Works of Tselinograd Medical Institute], Vol 3, 1969, pp 83-84.

4. Rakhal'skiy, L. B. Ibid, pp 93-94.

5. Bardina, R. A.; Dyskin, Ye. A.; and Tikhonova, L. P. in "Mezhdunarordnyy kongress anatomov. 9-y. Tezisy dokladov" [Summaries of Papers Delivered at the 9th International Congress of Anatomists], Moscow, 1970, p 227.

6. Bardina, R. A.; Bayko, G. F.; Lev, I. D.; et al. in "Vsesoyuznyy s"yezd anatomov, gistologov i embriologov. 8-y. Tezisy" [Summaries of Papers Delivered at 8th All-Union Congress of Anatomists, Histologists and Embryologists], Tashkent, 1974, p 39.

7. Bayko, G. F.; Lev, I. D.; and Shadrina, N. S. in "Ukrainskaya resp. konf. anatomov, gistologov i embriologov. 7-ya. Tezisy dokladov" [Summaries of Papers Delivered at the 7th Ukrainian Republic Conference of Anatomists, Histologists and Embryologists], Khar'kov, 1976, p 11.

8. Yevloyev, S. I. in "Tselinograd. med. in-t. Nauch. konf. 1-ya. Materialy" [Proceedings of First Scientific Conference of the Tselinograd Medical Institute], Tselinograd, 1967, pp 65-66.

9. Yevloyev, S. I.; Klebanov, V. M.; and Mikhaylov, S. S. in "Mezhdunarodnyy kongress anatomov. 9-y. Tezisy dokladov," Moscow, 1970, p 229.

10. Prives, M. G.; Astakhova, V. V.; and Stepantsov, V. I. ARKH. ANAT. [Archives of Anatomy], No 5, 1970, pp 32-37.

11. Mikhaylov, S. S.; Klebanov, V. M.; and Yevloyev, S. I. Ibid, No 11, 1971, pp 37-47.

12. Oganesyan, T. G. in "Vliyaniye nekotorykh fizicheskikh i biologicheskikh faktorov na organizm" [Effects of Some Physical and Biological Factors on the Body], Moscow, 1965, pp 74-80.

13. Golev, V. P., and Chepelenko, G. V. ARKH. ANAT., No 11, 1971, pp 47-49. pp 47-49.

14. Tikhonova, L. L.; Konkin, I. F.; and Zlatitskaya, N. N. in "Vsesoyuznyy s"yezd anatomov, gistologov i embriologov. 8-y. Tezisy," Tashkent, 1974, p 373.

15. Konkin, I. F. ARKH. ANAT., No 7, 1975, pp 33-35.

16. Sudzilovskaya, Ye. F. Ibid, No 1, 1972, pp 95-96.

17. Klebanov, V. M., and Brindzyuk, V. P. "Trudy Tselinograd. med. in-ta," Vol 3, 1969, pp 91-92.

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STUDIES OF PROGNOSTIC SIGNIFICANCE OF ANTIORTHOSTATIC POSITION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 48-54

[Article by Kh. Kh. Yarullin, V. A. Gornago, T. D. Vasil'yeva and M. Ye. Gugushvili, submitted 19 May 78]

[English abstract from source]

The prognostic significance of head-down tilt at −15° and −30° for 6 min at each step was assessed in 40 normal men, aged 22–39. The study of mean values of the maximal amplitude, relative duration of the anacrotic phase, dicrotic and diastolic indices of hemispheric and bimastoidal rheoencephalography as well as of health condition helped to determine cerebral circulation in test subjects with good and moderate tolerance to head-down tilt and to define the criteria of tilt tolerance. The test subjects who showed good tolerance to head-down tilt displayed a simultaneous compensatory increase of the tone of large caliber arteries and arterioles that was accompanied by a noticeable increase in cerebral pulse blood filling at −15° and a moderate increase at −30° as well as the feeling of a slight blood rush to the head. The test subjects who displayed moderate tolerance to head-down tilt showed only an increase in the tone of large caliber vessels; they also exhibited a marked decrease in the tone of arterioles, venules and veins (especially at −30°) which was combined with a significant increase in the cerebral pulse blood filling and an appearance of marked venous waves on rheoencephalograms.

[Text] Rheographic studies of regional hemodynamics with an antiorthostatic [head-down tilt] test on crew members of Soyuz-12, Soyuz-13 and the Salyut-4 orbital station revealed that this test can be used to predict resistance of the circulatory system to weightlessness and, in the postflight period, to determine the degree of adjustment of the cardiovascular system to space flight conditions [1-6]. In addition, there is particularly distinct demonstration of the effect of hydrostatic pressure of the column of blood on central autonomic nerve elements in antiorthostatic position, which could also be used to assess self-regulation of cerebral circulation. Yet little study has been made of a number of questions dealing primarily with criteria for assessing endurance of the antiorthostatic test.

Methods

The antiorthostatic load constituted one-half the passive postural test on a turntable, and it consisted of two successive tilts to 15 and 30° from the horizontal plane, with the head down for 6 min in each position. Rheograms were recorded on a 4-channel 4RG-1M rheograph. The operating frequency of the rheograph was 120 kHz, current of 2.5 mA and voltage of 3 V. The method, which is based on an alternating current demodulating bridge, is accurate to 10%. We recorded concurrently the rheoencephalogram (REG) in the fronto- and bimastoidal leads, rheograms (RG) of the right lung and leg, as well as the EKG in the second standard lead; we measured arterial pressure (according to Korotkov). The method for analysis of RG was described previously [7].

Results and Discussion

We studied the prognostic value of antiorthostatic position on 40 healthy males ranging in age from 22 to 39 years.

Comparative analysis of clinical condition and severity of REG changes in the first few minutes of head down position (due mainly to hydrostatic effects), as well as compensatory hemodynamic changes (which developed in the 3d-5th min of the test) enabled us to make a distinction between two groups of subjects: one with good (1st group) and the other with satisfactory (2d group) endurance of the test. Each group consisted of 20 men.

The mean values of background regional RG indices of the 2d group were indicative of normal tonus and pulsed filling of vessels of the brain, lungs and leg. There was some increase in arteriolar and veinous tonus in the basin of the internal carotid artery and vertebrobasilar system, which was evident from the fact that the top range of the age-related norm was somewhat exceed by the dicrotic (DCI) and diastolic (DSI) indexes on hemisphere and bimastoidal REG (Figures 1 and 2).

The heart rate was slower (by a mean of 3/min) in head-down position. There was virtually no change in systolic arterial pressure, whereas diastolic pressure rose by a mean of 14.2 mm Hg ($P<0.05$), without clear-cut differences between the two groups. Consequently, pulse pressure dropped somewhat.

In the first group of subjects, the increase in mean maximum REG amplitude for the right hemisphere did not exceed 38.9% ($P<0.02$) with -15° tilt and constituted 94.4% ($P<0.01$) with -30° tilt, as compared to the background (see Figure 1), whereas it reached 66.3 and 124.9% ($P<0.001$), respectively in the second group.

Mean relative duration of the anacrotic phase ($\alpha/T\%$) of the hemisphere REG increased more in the first group, reaching 59.8% with -15° ($P<0.02$)

and 162.1% with -30° ($P<0.001$). In the second group, α/T% increased by 49.4 and 62.0% ($P<0.01$), respectively (see Figure 1).

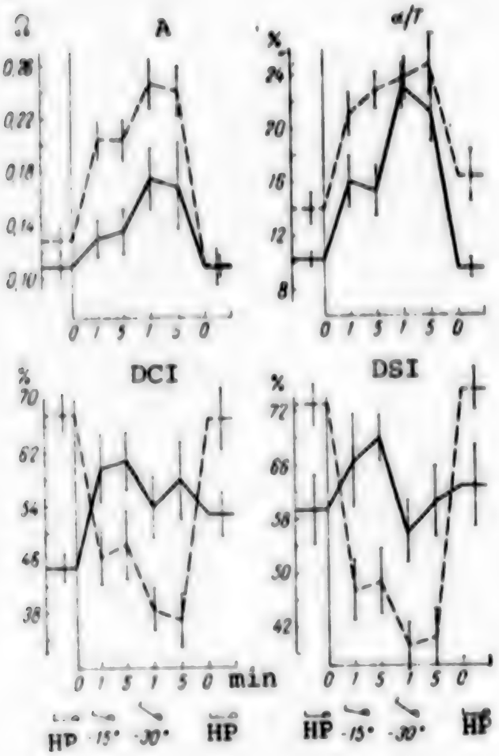

Figure 1.
Dynamics of mean values of maximum amplitude (A), α/T%, DCI and DSI on REG in right frontomastoid lead during stepped increases in head-down tilt, in the first (solid lines) and second (dash lines) groups

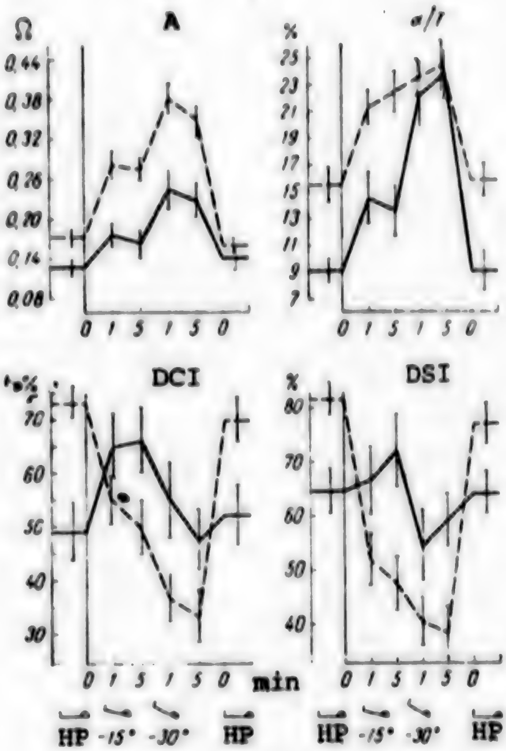

Figure 2.
Dynamics of mean values of maximum amplitude (A), α/T%, DCI and DSI on REG in bimastoidal lead during stepped increases in head-down tilt, in the first (solid lines) and second (dash lines) groups

In both figures: HP) horizontal position

There were more marked differences in changes of the REG dicrotic index between the first and second groups (see Figures 1 and 2). In the first group, there was an increase in mean DCI for the REG of the hemisphere to 35% ($P<0.05$) with a -15° angle and 12.1% with -30°, whereas in the second group the DCI dropped to 34.4 and 55.8%, respectively ($P<0.001$). Mean DSI of the hemisphere REG increased in the first group only with -15° tilt (to 11.4%), and decreased with -30°, but by no more than 15.1% ($P<0.5$) of the base value (see Figure 1); this parameter dropped by 41.6 and 52.8% ($P<0.01$), respectively, in the second group.

The increase in mean maximum amplitude of bimastoid REG in the first group did not exceed 24.1% ($P<0.5$) with -15° tilt and 61% ($P<0.02$) with -30° (see Figure 2); in the second group it reached 59.4 and 91.4% ($P<0.001$), respectively. The value of $\alpha/T\%$ rose in the first group to 56.6% with -15° and 125.9% ($P<0.001$) with -30°; in the second group, to 49.4 and 62.1% ($P<0.01$), respectively. In the first group, DCI on the bimastoid REG (as compared to hemispheric REG) increased more with the stronger factor, and reached 29.3% ($P<0.05$) with a tilt angle of -30°; its decline by 45.4% ($P<0.001$) in the second group was lesser than on hemispheric REG. As in the hemispheric REG, DSI rose only in the first group with a -15° tilt, reaching 14.3%; the decline was less marked than on the REG of the hemisphere, and did not exceed 35.1 and 46.5% ($P<0.001$), respectively.

During head-down position, there was some increase in pulsed filling of the right lung with blood, against the background of negligible decrease in tonus of large arteries and arterioles. In the second group, it decreased insignificantly, with concurrent slight increase in tonus of large vessels and decrease in arteriolar tonus. The changes in DSI, i.e., in tonus and pulsed filling of pulmonary veins, were minimal and also dissimilar.

There was an appreciable increase in pulsed delivery of blood to the leg in head-down position, to 35% of the base level in the first group and 28% in the second, against the background of elevation of arteriolar tonus (DCI, by 19.4 and 52%). However, these differences between groups, as those in the lung RG, were unreliable.

Thus, during stepped increase in angle of head-down tilt, we demonstrated reliable changes in indices of fronto- and bimastoid REG in both groups. We found a reliable difference between these groups of healthy subjects in mean DCI, DSI, maximum amplitude and $\alpha/T\%$ on hemispheric and bimastoid REG with tilt angles not only of -30° but -15°. The dynamics of these REG parameters indicate that concurrent compensatory increase in tonus of arterioles and arteries of large caliber, associated with significant increase in pulsed filling with -15° tilt and moderate with -30°, were inherent in individuals of the first group. The negligible decline of DSI, i.e., venous tonus, only with -30° also confirmed the rather effective counteraction of cerebral vessels to overfilling with blood. This state of compensated intracranial stasis was associated with some sensation of blood rushing to the head, pulsation in the temples, flushed face and injected scleral vessels.

In the second group of subjects, there was only marked increase in tonus of vessels of large caliber; the indices of tonus of arterioles (DCI), venules and veins (DSI) dropped appreciably, particularly with a -30° tilt angle, and they were not infrequently associated with appearance of distinct venous waves on the REG. This state of moderate arteriolar and venous stasis was associated with the sensation of marked rush of blood

to the head and even a feeling of cranial swelling ["bursting"], fever, pulsation of veins of the head, engorgement of cervical veins and hyperemia of the sclera, face and neck with a -30° tilt.

As we see, as compared to systemic and pulmonary hemodynamics, regional cerebral circulation reflects more specifically the compensatory and adaptational changes in regulation under the influence of antiorthostatic position. Dilatation of cerebral vessels leads to secondary increase in precapillary resistance and sphincter tonus, thereby counteracting dilatation and reduction in length of the open capillary bed [8], reducing to a minimum the signs of intracranial plethora. In other words, after the first minutes in head-down position with different tilt angles, the increasing venous stasis leads, by virtue of an arteriovenous reflex [9], to compensatory restriction of arterial influx to the brain [5, 10-12], due to increased tonus of vessels of large and medium caliber, as well as arterioles. This was indicated by the significant increase in α/T% and DCI.

As we know, maximum hydraulic resistance of the vascular system is referable to small arteries and arterioles [13-17]. In the brain, these vessels have a thick adventitia [muscular layer], and for this reason they play the role of the main element in regulation of cerebral circulation [17, 18]. Reduction of the lumen of precapillary arterioles has a more significant effect onvolumetric rate of cerebral blood flow than analogous changes in radius of other vessels [17]. This is the reason for the great informativeness of REG DCI, which reflects mainly the tonus of arterioles [7, 17, 19-23] as a criterion of endurance of head-down position associated with changes in perfusion and transmural pressure. Systemic and particularly regional arterial pressure is maintained chiefly by the arterioles with the use of postural factors [2, 5, 24, 25].

In the opinion of G. I. Mchedlishvili [11], the constrictive reaction of great vessels and, in part, pial arteries is the compensatory mechanism that prevents development of venous stasis in the brain, in addition to the system of collateral circulation. This was manifested on the REG of subjects in both groups by a drastic increase in α/T%, the indicator of tonus of large and medium caliber arteries [7, 19, 20], which is directed toward attenuating the excessive cerebral hyperemia. This is why α/T% was also an informative criterion of endurance of antiorthostatic position.

The effectiveness of the above mechanisms, which counteracted plethora of cerebral vessels, was distinctly manifested in the first group of subjects, whereas in the second group there was merely a significant increase in tonus of large and medium caliber vessels, with concurrent appreciable decrease in tonus of cerebral arterioles, venules and veins. The gradual decline of transmural pressure in cerebral vessels elicited moderate autoregulatory dilation thereof in order to maintain cerebral blood flow [26].

However, with such cerebral vasodilatation, even a minor elevation of systemic arterial pressure could cause further elevation of intracranial pressure, and it could be a factor that damages brain tissue [27]. Consequently, the demonstrated hypotonia of cerebral arterioles and veins, associated with subcompensated venous stasis in the brain, is indicative of some weakening of mechanisms of self-regulation of cerebral circulation in antiorthostatic position [2, 5, 28, 29], i.e., diminished functional capabilities of the cardiovascular system of subjects in the second group, as compared to the first. This confirms the prognostic value not only of DCI, but DSI on the REG, the indices of venous tonus and efflux, in head-down position [7, 10, 17, 19, 20, 30]. Constriction of cerebral veins, along with constriction of arterioles, diminishes influx of blood and capacity of the cerebral venous system [12, 31], thus stabilizing cerebral circulation [16].

As we see, the dynamics of α/T%, DSI and particularly DCI, as well as of maximum REG amplitude, which provide objective data on differences in endurance of head-down position, could serve as a reliable prognostic criterion for evaluation of the state of antigravity compensatory mechanisms of the cerebrovascular system as related to different postural tests. The dynamics of maximum REG amplitude, which reflects the pulsed increment in delivery of blood to the brain, make it possible to determine the severity of plethora in head-down position. The dynamics of α/T%, DCI and DSI, which reflect tonus of large arteries, precapillary and postcapillary vessels (arterioles, venules and veins), respectively, permit determination of the nature of cerebral hemodynamic changes during such tests.

Analysis of the dynamics of mean values for this indices of hemispheric and bimastoid REG's, as well as the physical condition of the subjects, enabled us to describe cerebral circulation in the case of good and satisfactory endurance of head-down tilting at angles increasing in steps, and to define the criteria of endurance of this test.

The criteria of good endurance of stepped increases in angle of head-down position are as follows: good subjective tolerance of the test (sensation of slight rush of blood to the head, pulsation of the temples, flushed face and erythremic sclera); appreciable elevation of DCI, the indicator of tonus of small arteries and arterioles (by 35% of the base level); increase in α/T%, the indicator of tonus of vessels with large and medium caliber by over 100%; increased pulsed delivery of blood, by 100% to the hemisphere and by 60% to the vertebrobasilar system; elevation or absence of change in DSI, index of tonus of venules and veins.

The criteria of satisfactory endurance of the test are: some discomfort (sensation of rush of blood and "bursting" in the head, fever, pulsation of veins, swelling of cervical veins, hyperemia of the face, sclera and neck); visible decrease in tonus of arterioles and small

arteries (DCI, by 28-55%); visible decrease in venous tonus (DSI, by 35-52%); increase to 80% in α/T%; increased pulsed delivery of blood, by more than 100% to hemispheres and more than 80% to the vertebrobasilar system.

The above criteria indicate that this test can be used to assess the functional capabilities of the cardiovascular system and efficiency of its antigravity mechanisms, i.e., to predict antiorthostatic stability of the body. This prompted us to use the test in screening cosmonaut candidates, as well as in preflight and postflight examinations of cosmonauts. The findings of the latter confirmed the efficacy of this test both to predict resistance of the circulatory system, particularly cerebral hemodynamics, to weightlessness, and to determine the nature and degree of changes in regulation thereof under the influence of space flight factors [2-5]. Since antiorthostatic position restricts, as we have shown above, the range (top) of self-regulation of cerebral circulation, the REG dynamics during this test can aid in detection of latent functional deficiency, primarily of its regulatory mechanisms.

BIBLIOGRAPHY

1. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. N.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1976, pp 3-18.

2. Yarullin, Kh. Kh.; Vasil'yeva, T. D.; Krupina, T. N.; et al. Ibid, No 2, pp 22-30.

3. Kalinichenko, V. V.; Asyamalov, B. F.; and Zhernavkov, A. F. Ibid, No 5, pp 18-23.

4. Kakurin, L. I., et al. in "Kosmicheskiye polety na korablyakh 'Soyuz.' Biomeditsinskiye issledovaniya" [Space flights Aboard Soyuz Series Spacecraft. Biomedical Studies], Moscow, 1976, pp 230-265.

5. Yarullin, Kh. Kh., and Vasil'yeva, T. D. KOSMICHESKAYA BIOL., No 3, 1977, pp 20-26.

6. Alekseyev, D. A.; Yarullin, Kh. Kh.; Krupina, T. N.; et al. Ibid, No 5, 1974, pp 66-72.

7. Yarullin, Kh. Kh.; Krupina, T. N.; and Vasil'yeva, T. D. Ibid, No 4, 1972, pp 33-39.

8. Folkov, B., and Nilk E. "Circulation," Moscow, 1976.

9. Wamada, S., and Burton, A. C. J. APPL. PHYSIOL., Vol 6, 1954, pp 501-505.

10. Moskalenko, Yu. Ye.; Vaynshteyn, G. B.; and Kas'yan, I. I. "Intracranial Circulation in the Presence of Accelerations and Weightlessness," Moscow, 1971.

11. Mchedlishvili, G. I. "Cerebral Arteriospasm," Tbilisi, 1977.

12. Kholodenko, M. I. "Venous Circulatory Disorders in the Brain," Moscow, 1963.

13. Savitskiy, N. N. "Some Methods of Studying and Making a Functional Assessment of the Circulatory System," Leningrad, 1956.

14. Wiggers, K. "Dynamics of Circulation," Moscow, 1957.

15. Burton, A. C. "Physiology and Biophysics of the Circulation," Chicago, 1965.

16. Kislyakov, Yu. Ya. "Mathematical Modeling of Cerebral Circulation and Exchange of Gases," Leningrad, 1975.

17. Sokolova, I. V.; Yarullin, Kh. Kh.; Maksimenko, I. M.; et al. ZH. NEVROPATOL. I PSIKHIATR. [Journal of Neuropathology and Psychiatry], No 9, 1977, pp 1314-1321.

18. Fog, M. J. NEUROL. PSYCHIATR., Vol 1, 1938, pp 187-197.

19. Yarullin, Kh. Kh. in "Klinicheskaya neyrofiziologiya" [Clinical Neurophysiology], Leningrad, 1972, pp 544-559.

20. Eninya, G. I. "Rheography as a Technique for Evaluating Cerebral Circulation," Riga, 1973.

21. Donzelot, E.; Milovanovich, J. B.; and Meyer-Heine, A. ARCH. MAL. COEUR [Archives of Heart Disease], Vol 11, 1950, pp 1013-1016.

22. Chlebus, H. AM. HEART J., Vol 64, 1962, pp 22-32.

23. Mukhamedrakhimov, F. F. EKSPER. KHIR. [Experimental Surgery], No 3, 1966, pp 10-13.

24. Samueloff, S. L.; Browse, N. L.; and Shepherd, J. T. J. APPL. PHYSIOLW, Vol 21, 1966, pp 47-54.

25. Kupriyanov, V. V.; Karaganov, Ya. L.; and Kozlov, V. I. "The Microcirculatory System," Moscow, 1975.

26. Kety, S. S. in "Handbook of Physiology, Sect. 1: Neurophysiology," Washington, Vol 3, 1960, pp 1751-1760.

27. Hamer, J., et al. J. NEUROSURG., Vol 46, 1977, pp 36-45.

28. Lassen, N. A. CIRCULAT. RES., Vol 15, Suppl 1, 1964, pp 201-204.

29. Meyer, J. S., et al. STROKE, Vol 4, 1972, pp 187-200.

30. Meyer-Heine, A.; Giblin, S.; and Dessertenne, G. ARCH. MAL. COEUR, Vol 42, 1949, pp 337-351.

31. Johnson, J. H., and Rowan, J. O. J. NEUROL. NEUROSURG. PSYCHIAT., Vol 37, 1974, pp 392-402.

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EVALUATION OF EFFICACY OF THE SET OF PREVENTIVE MEASURES REFERABLE TO THE HUMAN NEUROMUSCULAR SYSTEM UNDER HYPOKINETIC CONDITIONS

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[Article by V. A. Tishler, V. I. Safonov and Z. A. Krivitsina, submitted 4 Jan 79]

[English abstract from source]

The study of excitability and lability of the musculus rectus femoris was used to evaluate efficiency of exercises during bed rest. A combination of exercises with other countermeasures did not reduce their prophylactic effect

[Text] The results of medical studies conducted on the Salyut and Skylab programs revealed that the physiological changes occuring under the influence of flight factors can be adequately compensated and prevented with various preventive agents [1-7].

The fact that changes occur in the same direction after space flights and ground-based model experiments simulating some of the physiological effects of weightlessness makes it possible to evaluate various preventive measures on the model of hypokinesia [8, 9].

Many researchers believe that physical exercise is an effective means of preventing hypokinetic disorders [10-14].

Our objective here was to assess the efficacy of physical exercise (both by itself and in conjunction with other preventive steps) on the basis of excitability and lability of skeletal muscles in the course of 49 days of antiorthostatic (head-down) hypokinesia (ANOH).

Methods

Excitability and lability of the neuromuscular system (NMS) were tested by the method of electrostimulation, which was described in detail

previously [15]. We determined the excitation threshold, i.e., the rheobase, as well as optimum and maximum rhythm of stimulation of the femoral rectus muscle, twice in the background period, then on the 5th, 19th, 33d and 47th days of ANOH (-4°). In the first series of tests (6 people), the subjects exercised on a combination athletic exercizing unit (CAE) to prevent hypokinetic disorders. In the second series (6 people), in addition to physical exercise (on the CAE), we used conditioning with creation of lower body negative pressure (LBNP), and the subjects were given fluid and salt supplements (NaCl + H_2O).

In the third series (6 people), hypokinetic disorders were corrected by means of a set of preventive measures (exercise on the CAE, with LBNP, intake of water and salt supplement). In addition, pharmacological agents were used: 20 mg ephedrine and 1 mg strychnine daily given to all 6 subjects from the 15th to 25th days, and to 3 of them from the 39th to 49th days. L. I. Kakurin et al. [9] described in detail the preventive steps taken in the first, second and third series of tests. The fourth series (36 people) was a control (no preventive steps taken).

Results and Discussion

The dynamics of the rheobase of the femoral rectus muscle, illustrated in Figure 1, for all four series indicate that there was the same direction of changes in all series where preventive steps were taken. The highest, but insignificant elevation of threshold of stimulation was observed in the middle of the period of hypokinesia, on the 19th day for subjects in the 1st-3d series and 33d day in the 1st and 2d series. At the end of the hypokinetic period, excitability of the femoral rectus increased, to approximately the base value in the 1st and 2d series, and even somewhat higher in the 3d series. Unlike this, the decline of excitability in subjects of the 4th series progressed substantially with increase in duration of hypokinesia.

A comparative analysis of the parameters characterizing the lability of the NMS in subjects who only exercised on the CAE, with the use of the set of preventive measures and without them is illustrated in Figures 2 and 3.

Figure 2 shows that the optimum rhythm of stimulation of the femoral rectus changed insignificantly during hypokinesia in subjects of the series where preventive measures were used. A maximum tendency toward decline of this parameter was observed on the 5th day of hypokinesia in subjects for whom a set of preventive measures was used without pharmacological agents (by 16%, as compared to the base value). On the 19th, 33d and 47th days of hypokinesia, the tendency toward decline was more marked in subjects who only exercised on the CAE (by 10, 11 and 4%, respectively). In individuals who were submitted to the set of preventive measures without pharmacological agents, the optimum rhythm

of stimulation decreased by 3% on the 19th day of hypokinesia, as compared to the base level, whereas in the series where pharmacological agents were used it increased by 2%. Conversely, on the 33d day of hypokinesia, this parameter decreased by 8% with the use of pharmacological agents, and it increased by 4% in the series without such agents. On the 47th day of hypokinesia, the optimum rhythm of stimulation increased by a mean of 3% in both series where the complex of preventive measures was used. In contrast, the optimum rhythm of excitation in the 4th series of subjects began to decline on the 5th day of hypokinesia, constituting 50% of the base level on the 47th day thereof.

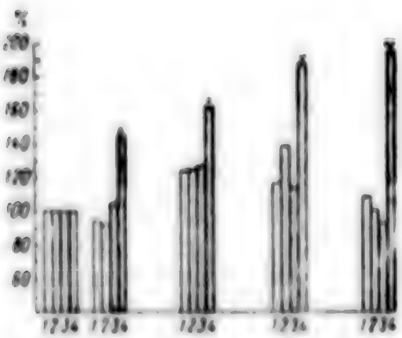

Figure 1.
Dynamics of relative change in rheobase of femoral rectus (base data--100%). Here and in Figures 2 and 3: 1-4) 1st, 2d, 3d and 4th series The "x" refers to reliable data ($P<0.05$). DH--day of hypokinesia; BG--background.

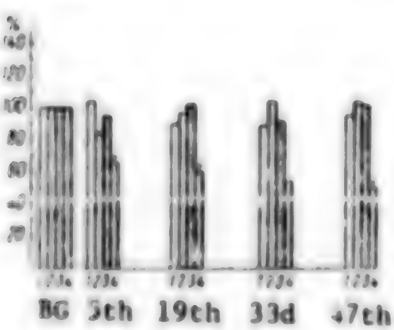

Figure 2.
Dynamics of relative change in optimum rhythm of femoral rectus (base data--100%)

Figure 3 illustrates the dynamics of maximum rhythm of excitation of the femoral rectus in subjects of all four series. There was the least decrease in maximum rhythm in subjects who only exercised on the CAE, and on the 5th, while on the 5th and 33d days of hypokinesia it even exceeded the base level (by 17 and 3%, respectively). The changes in maximum rhythm of excitation were about the same on the 19th and 33d days of hypokinesia in the subjects for whom a set of preventive measures was used. On the 5th and 47th days of hypokinesia, maximum rhythm declined more in the series with the set of preventive measures without pharmacological agents, and this decline was substantial on the 5th day of hypokinesia.

Thus, comparative analysis of changes in excitability and lability of the neuromuscular system of subjects referable to the four series demonstrated significant differences between the series where preventive steps were taken and where they were not. In the fourth series, excitability and lability diminished significantly starting on the 5th day of hypokinesia. In the series with use of preventive measures, the changes were insignificant, with the exception of the decrease in maximum rhythm of excitation on the 5th day of hypokinesia

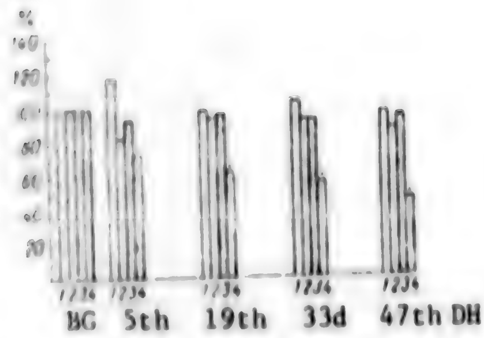

Figure 3.
Dynamics of relative changes in maximum rhythm of the femoral rectus (base data--100%)

in subjects of the first and second series, that could not be attributed to the preventive measures, since LBNP and the fluid and saltsupplement were not used at the first stage of hypokinesia.

Comparative analysis of parameters characterizing excitability and lability of the NMA of subjects who only exercised on the CAE, as well as those who followed the sets of preventive measures, revealed that these parameters undergo essentially insignificant changes during hypokinesia.

Retention of excitability and lability of the NMA, which was found in this study, along with retention of force of flexor and extensor muscles (10 muscle groups were tested), leads us to the conclusion that physical exercise is the chief means of preventing hypokinetic disorders of the NMA. Combination thereof with other preventive measures modifies insignificantly, but does not attenuate the preventive effect of exercising the human NMA.

BIBLIOGRAPHY

1. Vasil'yev, P. V. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 278-296.

2. Genin, A. M., and Pestov, I. D. in "Chelovek v kosmose" [Man in Space], Moscow, 1971, p 6.

3. Idem, Ibid, 1974, pp 76-90.

4. Pestov, I. D., and Asyamolov, B. F. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1972, pp 59-64.

5. Bestov, I. D., and Geratevol', Z. Dzh. in "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Moscow, Vol 2, Bk 1, 1975, pp 324-269.

6. McCally, N.; Piemme, T. E.; and Murray, R. H. AEROSPACE MED., Vol 37, 1966, pp 1247-1249.

7. McCally, M.; Pohl, S. A.; and Sampson, P. A. Ibid, Vol 39, 1968. pp 722-733.

8. Genin, A. M., and Kakurin, L. I. KOSMICHESKAYA BIOL., No 4, 1972, pp 26-28.

9. Kakurin, L. I.; Katkovskiy, B. S.; Tishler, V. A.; et al. Ibid, No 3, 1978, pp 20-27.

10. Brannon, E. W.; Kockwood, C. A.; and Potts, P. AEROSPACE MED., Vol 34, 1963, pp 900-906.

11. Yeremin, A. V.; Bazhanov, V. V.; Marishchuk, V. L.; et al. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 191-199.

12. Stepantsov, V. I.; Tikhonov, M. A.; and Yeremin, A. V. KOSMICHESKAYA BIOL., No 4, 1972, pp 64-68.

13. Idem, in "Nevesomost'," Moscow, 1974, pp 298-313.

14. Tishler, V. A.; Anashkin, O. D.; Pervushin, V. I.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 2, 1975, pp 190-192.

15. Titov, G. A. in "Problemy sportivnoy meditsiny. Metody vrachebno-fiziologicheskikh issledovaniy sportsmenov" [Problems of Sports Medicine: Methods of Medical and Physiological Studies of Athletes], Moscow, 1972, pp 35-40.

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THE STRESS REACTION TO HYPOKINESIA AND ITS EFFECT ON GENERAL RESISTANCE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 3, 1980 pp 57-60

[Article by I. P. Chernov, submitted 30 Sep 78]

[English abstract from source]

Rat experiments have demonstrated that the development of the hypokinetic syndrome involves occurrence of a three-stage stress-reaction characterized by a change in the general health state, body mass, and activity of the hypothalamic-pituitary-adrenal system. The hypokinetic stress affects total resistance and ionizing radiation sensitivity of animals. At a certain stage of development the hypokinetic stress contributes to the state of elevated "cross" resistance.

[Text] The data in the literature indicate that hypokinesia, which combines isolation and restricted muscular activity, elicits a stress reaction in man and animals [1-3]. It appears in response to depression of the "freedom instinct."

In this work, we have tried to trace the chronology of dynamic manifestations of the stress reaction on different levels of biological integration, and to demonstrate their correlation and influence on the body's general resistance.

Methods

Experiments were conducted on 250 male mongrel rats with an initial weight of 1[illegible]0-170 g. To create hypokinetic conditions, the animals were placed in box cages made of plexiglas, which restricted movement in all directions. We decapitated 6 rats from the experimental group and the same number from the control group after 3 h, 1, 3, 5, 10, 20, 30, 45, 60, 75 and 90 days. We evaluated the severity of stress and general resistance on the basis of the animals' general condition, weight (checked daily), condition of the system of the hypothalamus-hypophysis-

adrenals, and sensitivity to ionizing radiation. Proof of the informativeness of the indicators we selected has been offered in a number of works [4-6]. The rats were exposed to total-body radiation from a Luch unit (dosage 800 rad and dose rate 65 rad/min). The first group of animals was irradiated on the 3d day of hypokinesia, against the background of weight loss and significant elevation of 11-HCC [hydroxycorticosteroids] (to 13.83±0.002 μg%, versus 6.3±0.002 μg in the control). The second and third groups were exposed to radiation on the 20th day of hypokinesia and 3d day of the recovery period after 20-day hypokinesia, respectively. Rats kept in the vivarium prior to irradiation served as a control. On the 45th day, we determined the percentage of deaths and survivals in each group of animals. In all series of this study, we recorded the weight of the hypophysis and right adrenal. Karyometry of neurons of the arcuate nucleus of the hypothalamus and cells of the fascicular zone of the adrenals was performed on sections stained with cresyl violet. At each time, we measured 100 nuclei from each of 4 animals. We used an MOV-1-15^{x} ocular micrometer to measure the large (L) and small (B) diameters. The volume was determined using the following formula:

$$V = \frac{\pi}{6} LB^2$$

Weight and karyometric data were submitted to statistical processing [7, 8], and the reliability of differences was determined according to the criterion of Student (with $P<0.05$).

Results and Discussion

The rats were submitted to hypokinesia during the first days of brief motor excitement; on the next days (5th-10th days) we observed a decrease in motor activity, attenuation of the food reflex, diarrhea and shedding of fur. The animals then gradually adjusted to the new conditions, became more active, neat and consumed their feed willingly. In the 3d month of the experiment, we observed depression of motor activity and worsening of the animals' general condition.

The rats kept under the usual vivarium conditions gained weight progressively (Fiugre 1), reflecting prevalence of assimilation processes. Under hypokinetic conditions, the dynamics of body weight presented fluctuations: At the early stages weight dropped (with a peak on the 3d day), then it reverted to the base level (10th day), with subsequent (on the 10th-45th days) stabilization at slightly above base levels. In the 3d month of hypokinesia, body weight began to drop again. At the end of the experiment, the difference between wieght of experimental and control rats constituted 170 g.

The observed undulant changes in body weight and general condition of the animals during hypokinesia are typical of the stress reaction that occurs under the prolonged effect of deleterious factors. In particular,

such dynamics of rat weight were observed during prolonged, graduated electric stimulation [5]. The slower growth of animals with stress is attributed to impaired balance of metabolic processes in the direction of prevalence of dissimilation, dehydration of the body and mobilization of fat from the fat depots. All these changes inherent in stress have been repeatedly observed under hypokinetic conditions [9, 10].

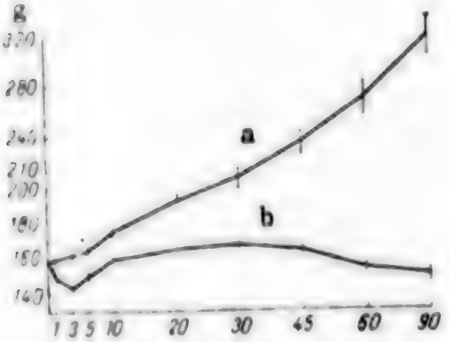

Figure 1.
Dynamics of weight change in control (a) and hypokinetic (b) rats; x-axis, day of examination; y-axis weight (g)

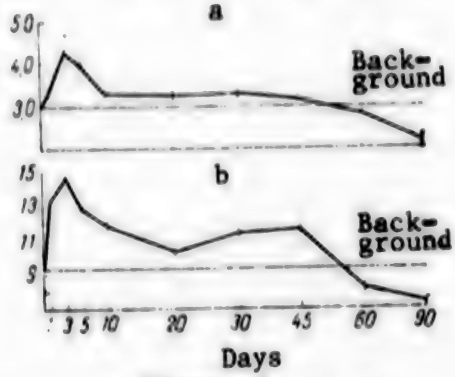

Figure 2.
Dynamics of relative weight of pituitary (a) and adrenals (b) under hypokinetic conditions; x-axis, day of examination; y-axis, weight (μg)/100 g body wt.

Analysis of relative weight of the hypophysis and adrenals revealed the same phasic nature as demonstrated for the animals' general condition and body weight (Figure 2), and this was clearly demonstrable on the tissular level. We must, however, indicate that the changes in weight of the pituitary and adrenals, as well as mean volume of neurons of the hypothalamic arcuate nucleus and cells of the fascicular zone of the adrenals, were in the opposite direction from those in body weight at the early stages of hypokinesia and in the same direction thereafter.

In view of the fact that the weight of endocrine organs is often correlated with function, while nucleus volume is a reliable criterion of secretory function of neurons [11] and the adrenal cortex [12], our conclusions pertaining to the phasic nature of changes in the hypothalamo-hypophyseo-adrenal system under hypokinetic conditions also extend to functional activity of this system. The nature and direction of changes in this system, as well as the fluctuations of body weight and general condition of the rats, indicate that a three-phase stress reaction develops in the course of formation of the hypokinetic syndrome, with periods of mobilization (first 10 days), resistance or "chronic resistance" (20-30 days) and a period of gradual depletion of the animals' potential for adjustment. The latter is manifested with particular distinction in the 3d month of the experiment. Such a chronology of hypokinetic stress was described by Ye. A. Kovalenko [3].

The fluctuations in general resistance under hypokinetic conditions were demonstrable when ionizing radiation was used as a test of rat sensitivity. Survival of rats exposed to radiation without additional factors (control group, 20 animals) constituted 30±10.1% by the 45th day, and death occurred at the height of radiation sickness (10th-20th days). The survival rate for animals exposed to radiation during the period of mobilization of hypokinetic stress (3d day, 26 animals) differed from the control without statistical reliability ($P>0.2$). However, the earlier death of animals in this group (mainly on the 5th-10th days) and slow weight gain by surviving rats (151±6.9 g on the 45th day, versus 200±5.0 g in the control) are indicative of some decrease in resistance to ionizing radiation during this period. The survival rate rose to 75±8.2% ($P<0.001$) and deaths occurred at a later time in the group of 28 rats exposed to radiation on the 20th day of hypokinesia. Such fluctuation of radiosensitivity of rats was demonstrated on the model of prolonged stress induced by graduated electrostimulation [5]. The authors showed that rat sensitivity to ionizing radiation increased at the stages of mobilization and depletion, and decreased at the resistance stage.

There are different mechanisms involved in formation of heightened "cross" resistance of the body associated with the stress reaction [13, 14]. It is important to note that it persisted for some time even after discontinuing exposure to the stimulus [15]. The latter thesis is consistent with our data, where increased resistance to radiation (exposure to radiation of 24 rats on the 3d day after 20-day hypokinesia; survival rate 58.3±10.1%) persisted during the period of readaptation.

Thus, in the course of formation of the hypokinetic syndrome, a three-phase stress reaction develops, which is manifested by the changes that are typical of this reaction: in general condition of the organism, body weight, activity of the hypothalamo-hypophyseo-adrenal system. Hypokinetic stress has a substantial effect on formation of general body resistance and its sensitivity to ionizing radiation. At a certain stage of its development, hypokinetic stress forms a state of heightened cross resistance.

BIBLIOGRAPHY

1. Portugalov, V. V.; Gazenko, O. G.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1967, pp 18-25.

2. Kosmolinskiy, F. P. "Emotional Stress During Work Under Extreme Conditions," Moscow, 1976.

3. Kovalenko, Ye. A. PAT. FIZIOL. [Pathological Physiology], No 3, 1975, pp 11-24.

4. Gorizontov, P. D. BME [Great Medical Encyclopedia], Moscow, Vol 1, 1976, pp 188-192.

5. Gorizontov, P. D., and Rudakov, I. A. PAT. FIZIOL., No 2, 1964, pp 17-22.

6. Aleshin, B. V. in "Gomeostaz" [Homeostasis], Moscow, 1976, pp 60-92.

7. Oyvin, I. A. PAT. FIZIOL., No 4, 1960, pp 76-85.

8. Khesin, Ya. Ye. "Size of Nuclei and Functional State of Cells," Moscow, 1967.

9. Seregin, M. S., et al. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 78-93,

10. Lobova, T. M. KOSMICHESKAYA BIOL., No 5, 1973, pp 32-35.

11. Polenov, L. A. "Hypothalamic Neurosecretion," Leningrad, 1968.

12. Palkovits, M., and Fischer, J. "Karyometric Investigations," Budapest, 1968.

13. Koronakis, P., and Selye, H. in "Pressing Problems of General Pathology and Pathophysiology," Moscow, 1976, pp 27-48.

14. Gorizontov, P. D. in "Gomeostaz," Moscow, 1976, pp 428-458.

15. Meyerson, F. Z. "General Mechanism of Adaptation and Prevention," Moscow, 1973.

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REGIONAL REDISTRIBUTION OF RAT BLOOD AFTER 7 AND 30 DAYS OF HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 60-64

[Article by O. A. Kovalev, V. F. Lysak, V. I. Severovostokova and S. K. Sheremetevskaya, submitted 28 Nov 78]

[English abstract from source]

An exposure of rats to hypokinesia was accompanied by a significant increase in the total amount of circulating blood per unit body mass. The percentage blood content was increased in the myocardium, lungs, liver, kidneys, small intestine, muscles and bones of the chest. The percentage blood content was decreased in the skin of different body segments, muscles and bones (except of the chest), tail, viscera (large intestine, adrenals, spleen, bladder, testes). The major regional redistribution of blood was its displacement into the liver.

[Text] The specific effect of "pure" hypokinesia can be studied in experiments on animals, the prolonged restriction of which is unrelated to changes in hydrostatic conditions.

We did not encounter publications in the literature accessible to us pertaining to the results of concurrent studies of absolute and relative fluctuations in filling of a rather large number of organs and tissues with blood under hypokinetic conditions. The only data published were obtained by morphological methods [1], which cannot be considered adequate to solve this problem. In this article, we describe the regional redistribution in circulating blood volume demonstrated with the use of radioisotopes in rats following 7 and 30 days of hypokinesia.

Methods

Experiments were conducted on nonanesthetized male rats weighing 180-200 g. The animals' appearance and behavior did not differ from normal. The rats

were conditioned to the laboratory situation, they became used to the experiment and allowed themselves to be held. Four days prior to the experiment, we introduced a catheter into the external jugular vein of animals under mild hexenal anesthesia (5-7 mg/100 g weight, intraperitoneally). The catheter was inserted under the skin in the occipital part of the head, and it was flushed twice a day with sterile 0.9% sodium chloride solution with heparin. The rats became used to our handling the catheter by the time blood volumes had to be analyzed. They were kept on the standard laboratory diet. We made the studies on a fasting stomach (last feeding 18-20 h before the experiment), but without restricting water intake, in order to minimize scatter of data related to the possible influence of the digestion process.

To produce hypokinetic conditions, the animals were put in very small cages with the body in the usual position. The cages were made of plexiglas, and they restricted significantly voluntary movements in all directions. We conducted three series of tests to study regional redistribution of blood: the first and second series involved keeping the animals in the small cages for 7 and 30 days; the third series served as a control. We used 14 rats in each series.

Changes in regional blood volume were studied in the following manner: intravenous injections were given to ^{51}Cr-labeled donor rat erythrocytes, as well as ^{131}I-labeled human serum albumins. The ratio of radioactivity of labeled formed elements to total activity of the tracer given to the animal equaled the value of individual blood hematocrit obtained when the tail was cut. The volume of injected tracer constituted 0.4 mℓ, and its total radioactivity was about 10 μCi. After uniform mixing of the tracer in the blood stream (10 min for labeled erythrocytes and 3 min for labeled plasma components), we induced cardiac arrest with an intravenous injection of 0.7 mℓ saturated KCl solution. The carcasses were frozen to -20°C for 2 h. Preparations were made of extracted organs and tissues to be studied. In each of the isolated specimens, we determined radioactivity, the level of which was proportionate to the amount of blood. We analyzed only differences between the control and experiment. There is evidence of the fact that the changes demonstrated by this method occurred before death, in spite of cardiac arrest induced by KCl [2].

Three series of experiments (11 rats in each) were conducted under analogous conditions to obtain the general characteristics of the model of hypokinesia. In these experiments, we measured pressure in the common carotid artery (AP) by the direct method, heart rate (HR) on the EKG, total circulating blood volume (TBV) by the method of dilution of ^{51}Cr-labeled erythrocytes and ^{131}I-labeled albumins. In addition to the parameters of systemic hemodynamics, we studied some parameters of carbohydrate metabolism, since impairment of the latter plays an important role in development of pathological changes under hypokinetic conditions [3]. We assayed lactic acid (LA), pyruvic acid (PA) content of blood, LA/PA ratio and lactic acid excess. We used conventional techniques [4, 5] to determine the parameters of carbohydrate metabolism.

When we analyzed the results, we evaluated the difference between mean values according to Student's t criterion. We used factor analysis in a modification that enabled us to supply a multidimensional description of changes between the control and experiment in order to characterize regional redistribution of blood [6]. We used an M-222 computer for statistical processing.

Results and Discussion

Table 1 lists the averaged values of parameters of systemic hemodynamics and carbohydrate metabolism for the control and experimental groups. The results are indicative of a statistically significant ($P<0.01-0.001$) increase in HR, TBV and appearance of lactic acid excess under the influence of hypokinesia. The changes in other parameters did not reach a level of statistical reliability. The increase in TBV (per unit weight) is consistent with data in the literature [7, 8]. This reaction was the opposite of the one demonstrated in other mammalian species and man, in which restricted motor activity induces a decrease in TBV [9].

Table 1. Some parameters of systemic hemodynamics and carbohydrate metabolism in hypokinetic rats

Parameter	Control	Hypokinesia				
		7 days		30 days		
	$M \pm m$	$M \pm m$	P_{1-2}	$M \pm m$	P_{1-3}	P_{2-3}
	1	2		3		
AP, mm Hg	121±2.20	124±3.10	>0.250	116±2.00	>0.100	>0.050
HR, per min	375±16.6	420±16.3	>0.050	464±14.2	<0.001	<0.010
TBV, mg/g weight	55±1.78	68±2.34	<0.001	73±4.36	<0.002	>0.500
Blood LA content, mmole/ℓ	1.86±0.26	2.54±0.32	>0.100	2.86±0.41	>0.050	>0.050
Blood PA content, mmole/ℓ	0.16±0.02	0.18±0.02	>0.250	0.17±0.03	>0.500	>0.500
LA/PA	11.6±1.42	14.1±1.46	>0.250	16.8±2.62	>0.050	>0.250
LA excess, mmole/ℓ	—	0.50±0.02	<0.001	0.90±0.05	<0.001	<0.001

On the whole, hypokinesia elicited relatively minor changes in parameters of systemic hemodynamics and carbohydrate metabolism. We failed to demonstrate significant metabolic disturbances that could have a marked local humoral effect on vascular tonus.

In view of the significant increase in TBV, the absolute blood content of all organs and tissues increased. Table 2 shows the significance of

Table 2. Changes in relative blood content (%TCB) in hypokinetic rat organs and tissues

Part of body	Tissues and organs	Control $M \pm m$	Rating, changes with hypokin. 7 days		30 days	
			P	f_1	P	f_1
Head	Skin	0.69±0.063	>0.500−	−0.337	>0.500+	−0.170
	Muscles and bones	3.68±0.202	>0.100−	−0.488	>0.250−	−0.402
	Brain	0.38±0.050	>0.500−	−0.218	>0.500+	−0.092
Neck	Skin	0.59±0.065	>0.250−	−0.302	>0.050−	−0.625
	Muscles and bones	2.76±0.284	>0.050−	−0.581	<0.020−	−0.625
Chest	Skin	1.77±0.123	>0.100−	−0.001	<0.010−	−0.385
	Muscles and bones	6.59±0.267	<0.002+	+0.024	<0.050+	+0.327
	Myocardium	1.60±0.154	<0.020+	+0.369	<0.050+	+0.593
	Lungs	7.60±0.579	0.050+	+0.161	<0.010+	+0.525
Abdomen and pelvis minor	Skin	1.63±0.278	>0.050−	−0.511	>0.050−	−0.158
	Muscles and bones	9.84±0.703	<0.001−	−0.395	<0.002−	−0.642
	Liver	36.1±1.227	<0.010−	+0.698	<0.050+	+0.536
	Small intestine	1.74±0.243	>0.250+	+0.255	<0.050+	+0.375
	Large intestine	1.56±0.134	<0.001−	−0.676	<0.001−	−0.687
	Stomach	0.70±0.097	>0.500+	+0.244	>0.500−	−0.050
	Kidneys	2.97±0.142	<0.020+	+0.479	>0.050+	+0.539
	Adrenals	0.10±0.011	<0.020−	−0.404	>0.100−	−0.259
	Spleen	3.84±0.843	<0.010−	−0.370	<0.002−	−0.578
	Pancreas	0.50±0.105	>0.500+	+0.162	>0.050−	−0.341
	Bladder	0.07±0.010	<0.001−	−0.534	<0.020−	−0.419
	Testes	1.38±0.100	>0.250−	−0.461	>0.100−	−0.262
Extremities: hind	Skin	0.37±0.069	>0.250−	−0.213	>0.500−	−0.194
	Muscles and bones	2.19±0.160	<0.001−	−0.642	>0.050−	−0.579
front	Skin	0.75±0.132	>0.100−	−0.258	>0.100−	−0.392
	Muscles and bones	3.26±0.319	>0.100−	−0.508	>0.500−	−0.323
	Tail	0.89±0.159	>0.250−	−0.530	>0.500	−0.212
Overall	Skin	5.32±0.348	<0.020−	−0.671	<0.002−	−0.772
	Muscles and bones	28.3±0.898	>0.250−	−0.662	>0.500−	−0.364
	Viscera	65.5±1.122	>0.100+	+0.705	>0.100+	+0.537
	Wt. of 1st factor, %	—	—	21.5	—	21.4
	Wt. of 2d factor, %	—	—	16.7	—	14.2

differences between mean values according to criterion t (P) and evaluation of factor load 1 (f_1). A "+" sign with the figures in the P and columns is indicative of relative increase in regional filling, as

compared to the control, while a "-" sign is indicative of decrease. The factor load was statistically significant ($P<0.05$) with an absolute value of ≥ 0.360. Factor load 1 is a quantitative characterization of the degree of interrelation between changes in each vascular region and changes in all other examined parts of the blood stream for this factor. The contribution of factor load 1 to the overall evaluation of differences between the experiment and control was of decisive significance.

The results listed in Table 2 indicate the following: Hypokinesia induced redistribution of blood in the liver, heart (myocardium), lungs, kidneys, small intestine, muscular and osseous tissue of the chest. There was a decrease in percentile blood content of the skin, muscle and bone tissues (with the exception of the chest), tail, some viscera (large intestine, adrenals, spleen, bladder, testes). Evidently, the main direction of regional changes was determined by redistribution of blood in the liver, which contains the largest share of TBV, as compared to other parts of the blood stream.

Similar regional redistribution of blood, with predominant shift into the liver, was observed in cases of hemorrhage against the background of anesthesia or immobilization, at the early stage following trauma in the presence of moderate cooling, and with infusion of excessive amounts of donor blood [10]. All this enables us to consider the redistribution of blood in the liver under hypokinetic conditions to be a nonspecific reaction. This reaction may be related to generalized constriction of capacitive vessels under the influence of nonspecific stimulation of the parasympathetic nervous system and hypothalamo-hypophyses-adrenal system under the influence of various stress agents [11, 12]. Evidently, the physiological purpose thereof is to mobilize the intravascular dynamic reserve localized in capacitive vessels [13, 14]. The blood mobilized for more active circulation is redistributed in organs and tissues, the functional activity of which is relatively increased under hypokinetic conditions as a result of diminished tonus of skeletal muscles: heart, lungs and muscles of the chest, liver, kidneys, small intestine. Perhaps, mobilization of blood from capacitive vessels is supplemented with more marked constrictive influences on resistive vessels of some parts of the skin, skeletal muscles and some of the abdominal viscera, which could also be instrumental in the above-described redistribution of blood. The results of physiological studies, which indicated quantitative dissimilarity of neurogenic constrictive influences of various parts of the blood stream on resistive vessels, are also in favor of this interpretation [15, 16]. Evidently, special studies are needed to identify the mechanisms of regional redistribution of circulating blood under hypokinetic conditions.

BIBLIOGRAPHY

1. Portugalov, V. V.; Savina, Ye. A.; Kaplanskiy, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1976, pp 19-24.

2. Kovalev, O. A. PAT. FIZIOL. [Pathological Physiology], No 3, 1977, pp 84-87.

3. Petrova, N. V., and Portugalov, V. V. KOSMICHESKAYA BIOL., No 5, 1977, pp 66-72.

4. Marbach, E. R., and Weil, M. N. CLIN. CHEM., Vol 13, 1958, pp 244-271.

5. Huckabee, W. J. CLIN. INVEST., Vol 37, 1958, pp 244-271.

6. Kovalev, O. A.; Nopochatov, O. N.; and Kolodyazhnyy, S. F. "Multidimensional Evaluation of the Resluts of Clinical and Experimental Studies Using a New Method Based on Factor Analysis. Lecture on Pathophysiology for Physicians," Leningrad, 1978.

7. Vasil'yev, P. V.; Uglova, N. N.; Volozhin, A. I.; et al. KOSMICHESKAYA BIOL., No 2, 1973, pp 13-173.

8. Krotov, V. P. "Kinetics and Regulation of Fluid-Electrolyte Metabolism in Hypokinetic Man and Animals," doctoral dissertation, Moscow, 1977.

9. Scholer, H. AM. HEART J., Vol 69, 1965, pp 701-712.

10. Kovalev, O. A. COR ET VASA (Prague), Vol 20, No 3, 1978, pp 230-238.

11. Chien, S. PHYSIOL. REV., Vol 47, 1967, pp 214-288.

12. Selye, H. AM. SCIENTIST, Vol 61, 1973, pp 692-699.

13. Folkow, B., and Mellander, S. AM. HEART J., Vol 68, 1964, pp 397-408.

14. Mason, D. T., and Bartter, F. C. ANESTHESIOLOGY, Vol 29, 1968, pp 681-692.

15. Khayutin, V. M. "Vasomotor Reflux [sic]," Moscow, 1964.

16. Tkachenko, B. I. in "Regionarnyye i sistemnyye vasomotornyye reaktsii" [Regional and Systemic Vasomotor Reactions], by B. I. Tkachenko, D. P. Dvoretskiy, V. I. Ovsyannikov et al., Leningrad, 1971, pp 257-270.

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SECRETION, INCRETION AND RESECRETION OF PANCREATIC LIPASE DURING PROLONGED RESTRICTION OF MOTOR ACTIVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 64-67

[Article by I. L. Medkova, N. M. Nikolayeva and K. V. Smirnov, submitted 22 Feb 79]

[English abstract from source]

The effect of 20, 60, 90 and 120-day hypokinesia on secretion, incretion and recretion of pancreatic lipase of rats was examined. It was found that 60, 90 and 120-day hypokinesia induced significant and similar changes — lipase decrease in the pancreas and increase in blood, bile, salivary glands and stomach mucosa; 20-day hypokinesia did not produce any effect on the above parameters.

[Text] In the last few years, new data have been obtained on the state of the digestive system in hypokinetic man and animals. Studies of man and animal experiments demonstrated changes in activity of a number of digestive enzymes responsible for hydrolysis of proteins, fats and carbohydrates [1-3]. Thus, activation of proteolytic enzymes and depression of carbohydrase activity were demonstrated under hypokinetic conditions of different duration. Yet there have been very few works published that deal with lipolytic enzymes when motor activity is restricted, and the information pertaining to activity of pancreatic lipase is fragmentary. However, there are indications that there is an increase in total lipid, cholesterol, β-lipoprotein and nonesterified fatty acid content of the blood under hypokinetic conditions [4-7]. Authors relate this process to mobilization of fat from the fat depots. In our opinion, this could also be the result of intensification of digestion of food fats in the gastrointestinal tract. It is known that the role of lipids as sources of energy in the body increases when motor activity is restricted and there is impairment of hydrolysis, transport and utilization of carbohydrates [4, 8].

Pancreatic lipase is the most important enzyme, which hydrolyzes chiefly long-chain triglycerides.

Pancreatic lipase is formed in acinar cells of the pancreas and passes with pancreatic juice into the duodenum, where the first stages of hydrolysis of alimentary fats occur. In addition, it passes into blood and lymph [9-17].

Pancreatic enzymes constantly circulate in the blood stream, and under normal physiological conditions their concentrations are maintained within a specific range [18-20]. This warrants reference to "exocrine-endocrine distribution" of products of secretory activity of the pancreas [21].

It is assumed that there is circulation of pancreatic enzymes between blood and the pancreas [22]. The enzymes entering the pancreas can then be resecreted with pancreatic juice [23]. It is believed that preservation of enzymes of pancreatic secretion by means of enteropancreatic circulation is important to preservation of energy for digestive processes.

The hypothesis has also been expounded that pancreated enzymes increted in blood may be significant to regulation of external secretory function of the pancreas, controlling synthesis and excretion of its enzymes by the feedback principle [16, 24]. In addition, the opinion is held that the physiological purpose of pancreatic enzymes that enter blood and lymph is involvement in interstitial metabolism [25, 26].

The level of lipolytic activity of blood depends primarily on the amount of lipase received from the pancreas, levels of excretion of lipase in urine, as well as resecretion ["recretion"] of the enzyme by different glands. In this case, recretion refers to the process of secretion of digestive enzymes from the blood by different organs, which are not producers of these enzymes. The recreted enzymes do not undergo appreciable conversions in the cell, and they are secreted in the same form as they came there. They can be involved in hydrolytic processes in the digestive tract [19, 20, 27]. Pancreatic lipase is resecreted by such glands as the gastric [19, 20, 28, 29], salivary [20, 29], intestinal [30, 31] and lactic [20].

Our objective here was to study secretion of pancreatic lipase by the pancreas, incretion thereof into blood and excretion of the enzyme by means of recretion by the salivary glands, glands of the stomach and liver as part of bile.

Methods

We conducted our studies on male, mongrel albino rats weighing 180-220 g. The animals were put in small, special hypokinetic cages for 20, 60, 90

and 120 days. We used 48 rats in all, 6 in the control and each experimental group. Cannulation of the common bile duct by the method used at the Institute of Nutrition, USSR Academy of Medical Sciences, was performed to obtain bile after hypokinesia. The animals were decapitated. We determined the activity of pancreatic lipase in blood serum, pancreatic tissue, gastric mucosa, salivary gland tissue and bile by the method of Myrtle and Zell [33] as modified by I. L. Medkova et al. [34]. This method was used to determine lipase activity, not only in blood, but other biological fluids and tissues. Studies of lipase activity in organs, tissues and media by the same method using the same substrate makes it possible to maintain that we are dealing with the activity of the same enzyme. We took 1 μmole of nonesterified fatty acids formed from the substrate per minute, scaled to 1 liter of blood serum, urine, bile or 1 g wet tissue of the pancreas, salivary glands or gastric mucosa, as the unit of lipase activity.

Results and Discussion

Restriction of the animals' motor activity for 20 days had virtually no effect on activity of pancreatic lipase. We only demonstrated a tendency toward increase in enzyme activity in blood serum, salivary gland tissue, gastric mucosa and bile against the background of an unreliable decline of activity in pancreatic tissue (see Table). Longer restriction of movement (60 days) induced marked changes in secretion and incretion of lipase, secretion thereof by the gastric mucosa and salivary glands, and with bile. On the 60th experimental day, there was a reliable decrease in lipase activity in pancreatic tissue. At this time its level in blood almost tripled. There was also reliable increase in secretion of lipase by salivary glands and in bile. Significant changes in recretion of lipase were noted in the gastric mucosa. Its activity was more than 20 times higher than the base level (see Table).

On the 90th day of hypokinesia, the changes in activity of pancreatic lipase in the above-mentioned organs presented the same dynamics as with 60 days of immobilization, but less marked. There was a reliable decrease in lipase activity in pancreatic tissue. However, incretion thereof, as well as content in the gastric mucosa and salivary glands, increased less significantly than in the case of 60-day hypokinesia. There was a reliable increase in secretion thereof with bile.

On the 120th day of hypokinesia, we demonstrated a reliable decrease in pancreatic lipase activity in pancreatic tissue, whereas its activity in blood serum almost doubled, as compared to the control level. There was an increase in secretion of pancreatic lipase by the salivary glands and with bile. Lipase activity increased to 1.71±0.19 units in the gastric mucosa, as compared to the control (0.51±0.21 units; $P<0.01$), which corresponds to almost threefold increase in recretion thereof by this part of the stomach.

Activity (in units) of pancreatic lipase (M±m) in different biological media with 20, 60, 90 and 120-day restriction of motor activity

Day of hypokinesia	Pancreatic tissue		Blood serum	
	control	experiment	control	experim.
20	1808.0±219.76	3731.0±284.53	99.4±20.19	102.2±9.80
60	8551.2±416.25	4202.4±442.98***	118.56±33.45	312.6±25.28***
90	6202.0±375.29	4304.0±391.4***	164.64±14.44	195.3±7.88
120	7462.0±411.75	6090.0±257.31*	132.3±19.3	279.23±23.35**

Day of hypokinesia	Gastric mucosa		Salivary gland tissue		Bile	
	control	experim.	control	experim.	control	experim.
20	0.98±0.12	1.46±0.45	0.2±0.068	0.22±0.1	504.0±73.95	551.0±121.3
60	0.01±0.0	0.202±0.016***	0.72±0.166	1.1±0.183	563.5±84.79	1186.5±149.26***
90	0.73±0.27	0.95±0.21	0.97±0.112	1.42±0.197	385.0±60.78	668.0±67.22**
120	0.51±0.21	1.71±0.19**	0.91±0.11	1.23±0.12	637.0±111.34	1008.0±115.28*

*P<0.02 (as compared to control) ***P<0.001
**P<0.01

Thus, the submitted results indicate that 20-day hypokinesia has virtually no effect on synthesis of pancreatic lipase, secretion thereof into blood and various digestive glands. Hypokinesia for 60, 90 and 120 days elicits significant changes, in the same direction, in lipase activity: reliable decrease in pancreatic tissue, significant increase in blood and redistribution in organs; intensified secretion by the gastric mucosa, salivary glands and with bile. The most profound changes occur with 60- and 120-day hypokinesia. The demonstrated correlation between secretion of lipase by various digestive glands and level thereof in blood is indicative of the recretory origin of the enzyme in these glands.

We did not consider all possible routes of elimination of the enzyme in our experiments. However, our findings are consistent with existing conceptions [19, 20, 29, 34] that enzymatic homeostasis of blood is provided by balanced incretion, as well as levels of renal and extrarenal excretion of the enzyme from the body.

As can be seen from the submitted data, high blood lipase levels on the 60th, 90th and 120th day of hypokinesia were associated with a reliable

decrease in its activity in pancreatic tissue. We assume that this may indicate intensified exosecretion of the enzyme into the duodenum against the background of normal synthesis thereof in the pancreas, on the one hand, and impairment of homeostatic function of the liver, when the enzyme level rises drastically in blood, while mechanisms of excretion and inactivation thereof are not adequately correlated, on the other hand.

The increase in pancreatic lipase content of digestive glands, which are not the sites of its synthesis, is a purposeful process directed toward stabilizing hydrolase level in peripheral blood serum and creation of optimum conditions for the most complete hydrolysis of lipids under hypokinetic conditions.

BIBLIOGRAPHY

1. Smirnov, K. V. "' tivity of the Digestive System During Exposure to Space Flight Factors," doctoral dissertation, Moscow, 1973.

2. Potemkina, L. S.; Goland, L. G.; Murashko, V. V.; et al. in "Fiziologiya i patologiya organov pishchevareniya" [Physiology and Pathology of Digestive Organs], Moscow, 1971, p 406.

3. Smirnov, K. V.; Goland, L. G.; Medkova, I. L.; et al. FIZIOLOGIYA CHELOVEKA [Human Physiology], No 4, 1976, p 653.

4. Lobova, T. M. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1973, p 32.

5. Parin, V. V.; Krupina, T. N.; Mikhaylovskiy, G. P.; et al. Ibid, No 5, 1970, p 59.

6. Bychkov, V. P.; Borodulina, I. I.; Gryaznova, V. N.; et al. in "Trudy 5-kh chteniy, posvyashchennykh razrabotke nauchnogo naslediya i razvitiyu idey K. E. Tsiolkovskogo. Sektsiya 'Problemy kosmicheskoy biologii'" [Transaction of 5th Lecture Series Dedicated to Development of the Scientific Legacy and Ideas of K. E. Tsiolkovskiy. Section on Problems of Space Biology], Moscow, 1971, p 132.

7. Goland, L. G. "Enzyme Secreting Function of the Pancreas During Exposure to Some Space Flight Factors," author abstract of candidatorial dissertation, Moscow, 1970.

8. Lobova, T. M., and Chernyy, A. V. KOSMICHESKAYA BIOL., No 6, 1977, p 36.

9. Boldyrev, V. N. RUSSK. VRACH [Russian Physician], No 2, 1914, p 45.

10. Milyushkevich, G. F. in "Nauchnaya konf. po problemam fiziologii i patologii pishchevareniya, posvyashchennaya pamyati akad. K. M. Bykova. Trudy" [Proceedings of Scientific Conference on Physiology and Pathology of Digestion Dedicated to the Memory of Academician K. M. Bykov], Ivanovo, 1960, p 547.

11. Dzhakson, I. M. "Exocrine Function of the Pancreas and Its Involvement in Regulation of Some Aspects of Metabolism," author abstract of doctoral dissertation, Leningrad, 1964.

12. Protsenko, V. A. "Effect of the Pancreas and Some Organs on Lipolytic Activity of Blood, Urine and Intestinal Juice," author abstract of candidatorial dissertation, Donetsk, 1964.

13. Kochnev, O. S., and Sharafislamov, F. Sh. in "Voprosy klinicheskoy khirurgii" [Problems of Clinical Surgery], Kazan', 1969, p 79.

14. Bartos, V.; Brzek, V.; and Groh, J. AM. J. MED. SCI., Vol 252, 1966, p 31.

15. Vega, R. E.; Appert, H. E.; and Howard, J. M. ANN. SURG., Vol 166, 1967, p 995.

16. Laporte, J.-C., and Tremolieres, J. C. R. ACAD. SCI. (Paris), Vol 273D, 1971, p 1205.

17. Papp, M., et al. EXPERIENTIA, Vol 33, 1977, p 1191.

18. Ugolev, A. M.; Iyezuitova, N. N.; Masevich, Ts. G.; et al. "Studies of the Human Digestive System," Leningrad, 1969.

19. Korot'ko, G. F. "Excretion of Enzymes by Gastric Glands," Tashkent, 1971, p 18.

20. Abdurakhmanov, Kh. Kh.; Vepritskaya, E. A.; Glushko, L. F.; et al. in "Vsesoyuznoye fisiologicheskoy o-vo im. I. P. Pavlova. S"yezd. 12-y. Referaty dokladov na simpoziumakh" [Abstracts of Papers Delivered at Symposiums of the 12th Congress of the All-Union Physiological Society imeni I. P. Pavlov], Leningrad, Vol 1, 1975, p 233.

21. Janowitz, H. D., and Hollander, F. GASTROENTEROLOGY, Vol 17, 1951, p 591.

22. Thomas, J. E. MED. CLIN. N. AMER., Vol 40, 1956, p 273.

23. Gotze, H., and Rothman, S. S. NATURE, Vol 257, 1975, p 607.

24. Leibow, C., and Rothman, S. S. SCIENCE, Vol 189, 1975, p 472.

25. Kretovich, V. L. "Introduction Into Enzymology," Moscow, 1967.

26. Dumont, A. E.; Doubilet, H.; and Mulholland, J. H. ANN. SURG., Vol 152, 1960, p 403.

27. Hirsch, J. C. in "Handbuch der Allgemeinen Pathologie," Berlin, Vol 2, No 1, 1955, p 92.

28. Inamova, K. B. "Amylase and Lipase in Secretions of Pyloric and Fundal Gastric Glands, and Possible Recretory Origin Thereof," author abstract of candidatorial dissertation, Tashkent, 1970.

29. Kamakin, N. F.; Abdurakhmanov, Kh. Kh.; Inamova, K. B.; et al. in "Mekhanizmy povrezhdeniya, rezistentnosti, adaptatsii i kompensatsii" [Mechanisms of Injury, Resistance, Adaptation and Compensation], Tashkent, Vol 2, 1976, p 34.

30. Gulyamov, T. K. "Compensatory and Adaptational Changes in the Small Intestine Under Different Functional Conditions," author abstract of doctoral dissertation, Tashkent, 1974.

31. Pulatov, A. S., and Glushko, L. F. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 3, 1977, p 452.

32. Korot'ko, G. F., and Kurzanov, A. N. Ibid, No 1, 1978, p 81.

33. Myrtle, J. F., and Zell, W. J. CLIN. CHEM., Vol 21, 1975, p 1469.

34. Medkova, I. L.; Smirnov, K. V.; Mazo, V. K.; et al. LABOR. DELO [Laboratory Record], No 3, 1978, p 142.

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THEORETICAL ANALYSIS OF THE EFFECT OF STATE OF PULMONARY CIRCULATION ON DISTRIBUTION OF VENTILATION-PERFUSION RELATIONS AND GAS EXCHANGE IN THE LUNGS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 68-71

[Article by A. I. D'yachenko and V. [illegible]l'nikov, submitted 24 Aug 79]

[English abstract from source]

Using a mathematical model of functionally nonuniform lungs, the effect of gravitational inequality of ventilation-perfusion relations on gas exchange was studied. The dependence of tensions of respiratory gases in the mixed arterial blood and alveolar air upon pulmonary circulation pressure was demonstrated. The influence of changes in the tone of lung vessels on the distribution of ventilation-perfusion relations and gas exchange was investigated.

[Text] As shown by experimental studies [1-3], the hemodynamic parameters of the pulmonary circulatory system have a substantial effect on degree of functional heterogeneity of the lungs. In particular, it was established that there is a marked correlation between arterioalveolar difference for carbon dioxide tension, which characterizes nonuniformity of ventilation-perfusion relations ($\dot{V}_A/\dot{Q}$) in the lungs, and pressure in the pulmonary artery [1]. Since the mechanism that determines this correlation is not quite understandable, our objective here was to make a quantitative study thereof by means of a mathematical model of functionally heterogeneous lungs, which was developed previously [4]. Our results enable us to assess the influence of possible changes in tonus of pulmonary vessels and blood pressure in them as a result of prolonged exposure to weightlessness on distribution of $\dot{V}_A/\dot{Q}$ and exchange of gases.

Methods

The mathematical model of functionally heterogeneous lungs consisted of three parts: models of blood flow, ventilation and gas exchange.

The blood flow model is based on analysis of the mechanics of stationary flow of liquid in an elastic vascular channel with proper dichotomic branching. Seven sections of the vascular bed are considered: 1) arterial reservoir; 2) extraalveolar arteries; 3) alveolar arteries; 4) capillaries; 5) alveolar veins; 6) extraalveolar veins; 7) venous reservoir. The resistance in sections 1 and 7, which are outside the pulmonary lobes, is considered as equal to zero. Blood pressure in them is hydrostatic. To describe the area of vascular cross section as a function of transmural pressure, we used approximation of empirical data [5, 6]. The equations for quasi-one-dimensional flow, written down for each section in a pulmonary lobe, were submitted to analytical integration. We obtained a system of equations which related blood flow Q, resistance of unstretched vessels R_i, elasticity of vessels α_i, and pressure at the start and end of the ith section. The equations describe vascular collapse with negative transmural pressure and stretching with positive transmural pressure.

We considered only nonuniformity of ventilation and blood flow due to +1 Gz acceleration. The lungs were divided into 10 horizontal layers. We numerically solved a system of equations describing blood flow and euqations of mechanics of pulmonary parenchyma [4] to calculate blood flow and ventilation in each layer.

Studies of the model of parenchymal mechanics revealed that the distribution of ventilation is related to blood volume in the lungs and changes therein in the course of a respiratory cycle. Thus, the hemodynamic parameters influence distribution not only of blood flow, but ventilation. This influence is more marked with increase in elasticity of the lungs and nonlinearity of the volume-transpulmonary pressure curve. In this study we used a slightly nonlinear volume-transpulmonary pressure curve for lungs with low elasticity [stretchability]. For this reason, the distribution of ventilation changes little with change in state of pulmonary circulation.

Using the calculated values of ventilation and blood flow, we numerically solved equations describing "ideal" exchange of gases [7] in each horizontal layer of the lungs. We used algorithms [8] to describe the link between concentrations of respiratory gases and their tension in blood. We calculated the gas composition of mixed arterial blood and mixed alveolar air, as well as ΔP_G: alveolar-arterial differences for oxygen tension ΔPO_2 and for carbon dioxide tension ΔPCO_2. Oxygen tension in venous blood was considered to be 40 mm Hg and that of carbon dioxide 45 mm Hg, i.e., we considered conditions of rest, tissular normoxia and normocapnia.

Results and Discussion

Tension of respiratory gases in blood and mixed alveolar air is related not only to nonuniformity of $\dot{V}_A/\dot{Q}$, but to the mean $\dot{V}_A/\dot{Q}$. A study was made

of the effect on gas exchange of an increase in mean $\dot{V}_A/\dot{Q}$ with constant distribution of $\dot{V}_A/\dot{Q}$ in relation to the mean, which corresponded to moderate voluntary hyperventilation. The estimates made for different gravitational nonuniformities of $\dot{V}_A/\dot{Q}$ revealed that with increase of mean $\dot{V}_A/\dot{Q}$ from 0.85 to 1.5, ΔPO_2 decreases by about 40%, while ΔPCO_2 increases by less than 0.2 mm Hg. For a stationary state at rest, mean $\dot{V}_A/\dot{Q}$ equals 0.85-1.0 [2, 3]. We also submit the results obtained for a mean $\dot{V}_A/\dot{Q}$ of 0.85, since in this case the influence of nonuniformity of $\dot{V}_A/\dot{Q}$ on gas exchange is at a maximum. Analysis of the model revealed that with a constant mean $\dot{V}_A/\dot{Q}$ the distribution of $\dot{V}_A/\dot{Q}$ does not depend on overall resistance of unstretched vessels R_T, but on R_i/R_T ratios.

We selected "normal" values of R_i and α_i on the basis of previously published data [5, 6, 9]. In accordance with the results obtained in [10], let us consider that a change in tonus of arterial vessels leads to a change in R_2 and R_3 with constant α_2 and α_3. According to the model equations, there is virtually no change in distribution of $\dot{V}_A/\dot{Q}$ when pressure in the arterial and venous reservoirs is constant. Consequently, a change in vascular tonus could affect gas exchange only if there is a change in pressure in the pulmonary circulation, in arteries (P_v) and veins (P_V).

We calculated distribution of $\dot{V}_A/\dot{Q}$ and gas exchange with different levels of mean pressure in the main pulmonary artery and pulmonary veins in the case of "diminished tonus" of arterial vessels (R_2 = 9 mm Hg/cm^3/s, R_3 = 8 mm Hg/cm^3/s) and "normal" other R_i, α_i. A comparison of the estimates made for "normal" and "diminished" tonus revealed that the ΔP_G gradient constitutes a few percentage points with the same pressure in the pulmonary circulation.

Figure 1 illustrates estimated and experimental curves of distribution of $\dot{V}_A/\dot{Q}$ over the height of the lungs. Figure 1 shows that the wide variability of the curves observed in our studies could be due to the difference in pulmonary artery pressure.

Figure 2 illustrates the effect of pressure changes in the pulmonary artery on exchange of gases. Estimates were made for a constant arteriovenous pressure gradient of 7.5 mm Hg. Figure 2 shows that CO_2 tension of arterial blood undergoes negligible change. ΔPCO_2 changes due to change in CO_2 tension in mixed alveolar air. This is consistent with experimental findings [1]. For oxygen, the opposite results are observed: ΔPO_2 changes more due to change in oxygen tension in arterial blood.

Figure 3 illustrates the influence of pressure in pulmonary veins and arteries on ΔP_G. We see that when pressure in the pulmonary circulation is high, and the lungs are entirely under the conditions of the third zone, ΔP_G is low. With decrease in pressure in the veins there is an increase in size of the second zone, and with decrease in pressure in the

main pulmonary artery (P_a^0) the first zone increases, which increases ΔP_G. ΔPCO_2 as a function of pressure in the main pulmonary artery was obtained [1] for accelerations of +1 Gx with the following regression equation:

$$\Delta PCO = (11.9 - 0.54 \cdot P_a) \text{ mm Hg.}$$

In spite of the difference in position of the body, there is a conformity between theoretical and experimental data.

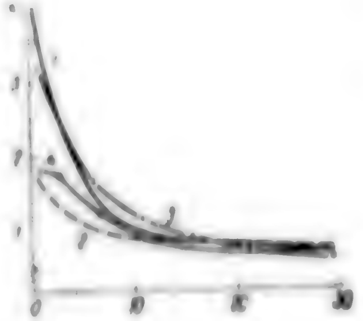

Figure 1.
Distribution of $\dot{V}_A/\dot{Q}$ over height of lungs. X-axis, distance from lung apices (cm); y-axis, $\dot{V}_A/\dot{Q}$
1, 2) theoretical curves
3, 4) experimental curves [2, 3]
For curve 1, blood pressure in common pulmonary artery is 16.5 mm Hg and pressure in pulmonary veins (left atrium) is 5.2 mm Hg. For curve 2, the respective pressures are 19.5 and 8.2 mm Hg. The distance between common pulmonary artery and veins to apices of the lungs is considered to be 18 cm.

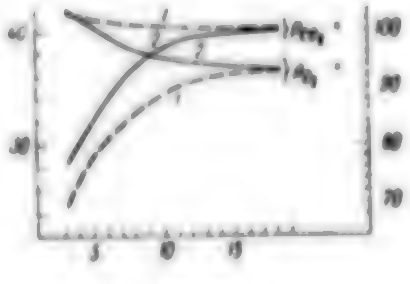

Figure 2.
Tension of respiratory gases in mixed arterial blood (1) and mixed alveolar air (2) as theoretical function of blood pressure in pulmonary artery; the "+" signs refer to "ideal lungs" [7]. X-axis, pressure in common pulmonary artery (mm Hg); y-axis; CO_2 tension (mm Hg) on the left and O_2 tension (mm Hg) on the right

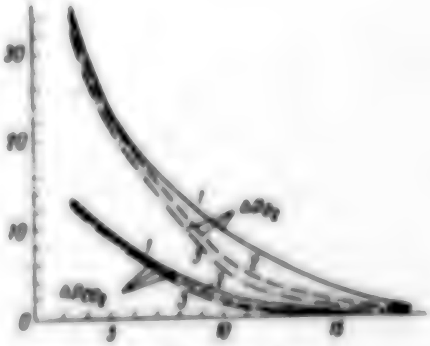

Figure 3.
ΔP_G as a theoretical function of blood pressure in common pulmonary artery. X-axis, blood pressure in common pulmonary artery (mm Hg); y-axis, ΔPO_2 and ΔPCO_2 (mm Hg).
1-3) arteriovenous blood pressure gradient of 11.3, 7.5 and 6 mm Hg

Blood pressure in the left atrium must be higher than in the lower part of the pleural cavity, i.e., over 2 mm Hg. At rest, blood flow through the lungs is at least 4 liters/min. Since R_T>100 mm Hg/cm^3/s, pressure in the main pulmonary artery must be over 5 mm Hg. Consequently, Figure 3 illustrates the maximum effect of gravitational nonuniformity on ΔP_G. In addition to gravity, there may be other causes of nonuniformity of $\dot{V}_A/\dot{Q}$, as well as an anatomical shunt, which increases ΔP_G [11]. However, in healthy lungs at rest, gravity is the chief cause of nonuniformity of $\dot{V}_A/\dot{Q}$ [1-3, 11].

If vascular tonus is constant over the height of the lungs, exchange of gases is determined by pressure in the pulmonary circulation and depends little on vascular tonus. But if complete blood flow and P_a-P_v remain constant with diminished tonus, the pressure in the pulmonary artery drops. This causes an increase in nonuniformity of $\dot{V}_A/\dot{Q}$ and ΔP_G. The question of quantitative changes in blood flow and pressure in the pulmonary circulation is beyond the scope of the model, since these changes depend on the state of systemic circulation. It must be noted that while a change in tonus leads to a change in α_ζ, distribution of $\dot{V}_A/\dot{Q}$ and exchange of gases change with constant pressure in the pulmonary circulation.

BIBLIOGRAPHY

1. Askrog, V. J. APPL. PHYSIOL., Vol 21, 1966, pp 1299-1306.

2. West, J. B. Ibid, Vol 17, 1962, pp 893-898.

3. Harf, A.; Pratt, T.; and Hughes, J. M. B. Ibid, Vol 33, 1978, pp 115-123.

4. Genin, A. M.; D'yachenko, A. I.; and Shabel'nikov, V. G. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Pt 1, 1979, pp 37-39.

5. Maloney, J. E.; Rooholamini, S. E.; and Wexler, L. MICROVASC. RES., Vol 2, 1970, pp 1-12.

6. Shapiro, A. M. TRANS. ASME, Vol K99, 1977, pp 126-147.

7. Rahn, H., and Fenn, W. O. "A Graphical Analysis of the Respiratory Gas Exchange (The O_2-CO_2 Diagram)," Washington, 1956.

8. Kelman, G. R. RESP. PHYSIOL., Vol 3, 1967, pp 111-115.

9. Milnor, W. R. in "Cardiovascular Fluid Dynamics," London, Vol 2, 1972, pp 299-340.

10. Ayvar, Yu. P., and Kalnin'sh, I. Ya. in "Vsesoyuznaya konf. po problemam biomekhaniki. 2-ya" [Second All-Union Conference on Problems of Biomechanics], Riga, Vol 1, 1979, pp 149-151.

11. Gledhill, N.; Froese, A. B.; Buick, F. J.; et al. J. APPL. PHYSIOL., Vol 45, 1978, pp 512-515.

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METHOD FOR ASSESSING HEMODYNAMICS AND DETECTING LATENT INSUFFICIENCY OF CEREBRAL CIRCULATION IN COSMONAUT CANDIDATES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 71-74

[Article by D. A. Alekseyev, submitted 9 Nov 78]

[Text] Experience in screening cosmonaut candidates shows that many of them present osteochondrosis of the cervical spine. In some of the selected individuals, the signs of intervertebral osteochondrosis are progressing. Osteophytes in this region sometimes cause ischemic circulatory disturbances in the vertebrobasilar system as a result of reflex angiospasm of vertebral arteries and mechanical compression of the latter [1-4]. For this reason, in expert screening of this group of candidates, it is very important to assess blood flow in the systems of the vertebral arteries (basilar and internal carotid), determine the functional capabilities of collaterals and latent circulatory disturbances in the corresponding vascular reservoirs. A functional test is used for this purpose, involving rotation of the head and throwing it back to an angle of 45° [5-10].

Methods

Cosmonaut candidates with osteochondrosis of the cervical spine (28 people ranging in age from 23 to 44 years) and 15 healthy volunteers 25-37 years of age (control group) rotated their head to the side to the maximum degree and threw it back to an angle of 45°. We recorded the EEG from 8 symmetrical points of the scalp (forehead, center, temple and occiput) synchronously with the REG [rheoencephalogram] (frontomastoid and occipitomastoid leads). Synchronous recording of the REG and EEG enabled us to determine the correlation between degree of decrease in delivery of blood to the brain and cerebral hypoxia that occurred [1, 7, 9, 11].

Results and Discussion

There was appreciable decrease in amplitude of the occipitomastoidal REG by 19.2-20.6% ($P<0.05$) on the side of the turn when individuals with

cervical osteochondrosis turned their head to the sides. When the head was thrown back, the reduction of pulsed delivery of blood to the basins of the vertebral and basilar arteries reached 23.1-27.3% ($P<0.001$), as compared to the background. These changes were less marked in the basin of the internal carotid artery (Figure 1). The decreased pulsed filling of cerebral vessels while turning the head and throwing it back was associated with significant adaptational redistribution of tonus of arteries and veins with large, medium and small caliber, most marked in the basin of the internal carotid, in individuals with early manifestations of osteochondrosis.

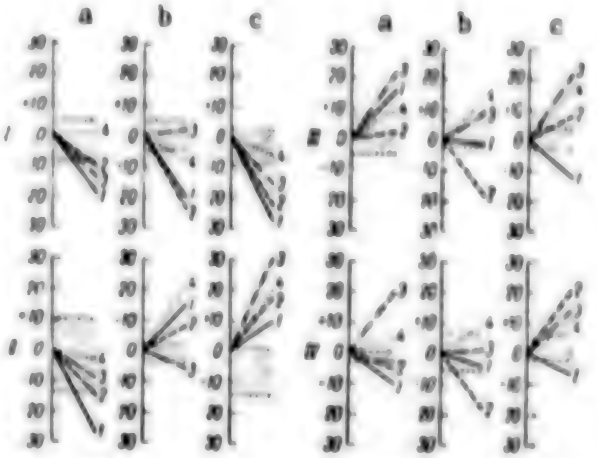

Figure 1. Dynamics of mean values of REG parameters (% of base levels) while turning the head and throwing it back, in individuals with early manifestations of cervical osteochondrosis. Striped areas show the range of fluctuation of REG parameters during functional tests on the control group of subjects

I) maximum REG amplitude
II) index α/T
III) diastolic index
1, 2) right and left occipitomastoidal REG
3, 4) right and left frontomastoidal REG
a) turn to the right
b) turn to the left
c) head thrown back

There was particularly significant increase in tonus of arteries and veins of different caliber when the head was thrown back, and this is apparently related to overstimulation of the vertebral nerve and cervical sympathetic plexus by the osteophytes [12-14]. The nitroglycerin test confirmed the predominantly reflex genesis of increased cerebrovascular tonus in individuals with osteochondrosis: under the influence of nitroglycerin

(0.00025 under the tongue) turning or throwing the head back no longer caused a decrease in pulsed delivery of blood or change in tonus of cerebral vessels. However, in some subjects, the deficient pulsed filling of the vertebrobasilar system on the side of the turn and when the head was thrown back persisted even with intake of nitroglycerin, and this was indicative of prevalence of mechanical effect of osteophytes on the vascular wall.

The most marked changes in dominant rhythm on the EEG were observed when the head was thrown back: appreciable increase in amplitude and index of α-rhythm, smoothing of zonal differences (Figure 2). These changes in the direction of hypersynchronization of bioelectrical activity when the head was turned and particularly when it was thrown back occurred in all subjects with early signs of cervical osteochondrosis and in eight subjects in the control group.

In addition, in 7 subjects with early manifestations of cervical osteochondrosis we observed appreciable increase in number of low-amplitude (to 35 μV) diffuse θ- and δ-waves on the EEG, against the background of decreased amplitude of dominant rhythm, i.e., "flattening" of the EEG, when turning the head in the direction of greatest decrease in pulsed filling (to 36% of the base level), i.e., of maximum deterioration of patency of the vertebral artery, as well as when the head was thrown back. Along with background α-activity, we recorded segments of low-amplitude (40-60 μV) slow (7-8 Hz) α-rhythm (Figure 3). Such EEG changes were not observed in the control group of subjects.

The decreased amplitude and index of dominant rhythm, as well as in diffuse low-amplitude slow activity on the EEG, were observed by V. A. Chukhrova in the presence of brief circulatory hypoxia [7].

Consequently, the observed synchronous changes in the REG and EEG during the functional test (appearance of moderate, diffuse changes in bioelectrical activity of the brain following appreciable decrease in pulsed delivery of blood to the vertebrobasilar system) are indicative of the circulatory ischemic nature of the above-mentioned electroencephalographic changes in subjects with early signs of cervical osteochondrosis. This is also confirmed by the appearance of reactive cerebral hyperemia immediately after the test involving tilting the head back. As we know, reactive hyperemia occurs in response to prior ischemia of cerebral tissue [15, 16]. Since this group of subjects had no subjective or objective clinical manifestations of disease, we could only be dealing with detection of latent insufficiency of circulation, inadequate delivery of blood to the vertebrobasilar system as a result of insufficient effectiveness of collateral circulation with the use of these functional tests (which temporarily limit blood flow to the vertebral arteries).

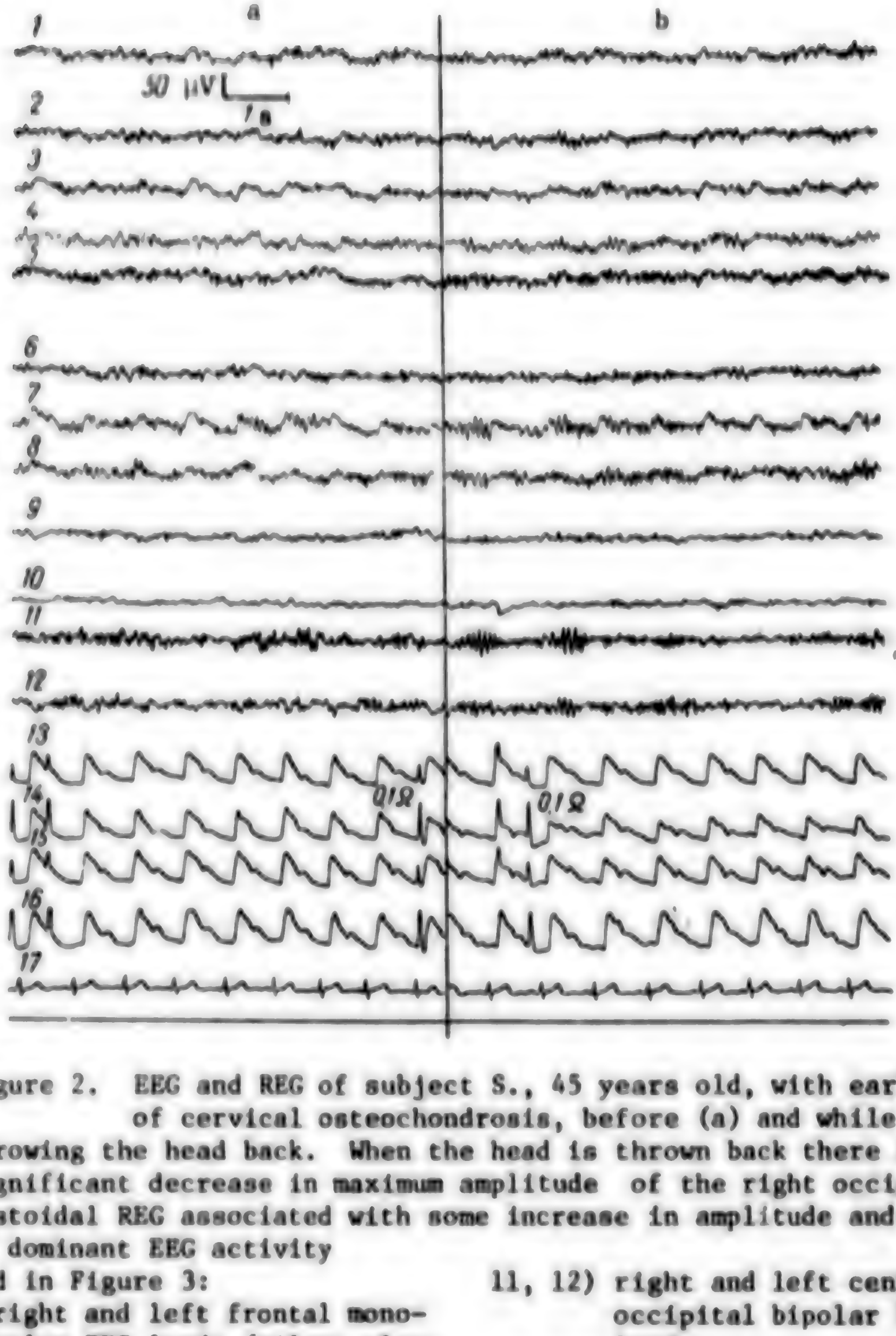

Figure 2. EEG and REG of subject S., 45 years old, with early signs of cervical osteochondrosis, before (a) and while (b) throwing the head back. When the head is thrown back there is significant decrease in maximum amplitude of the right occipito-mastoidal REG associated with some increase in amplitude and index of dominant EEG activity

Here and in Figure 3:

1, 2) right and left frontal monopolar EEG leads (silent electrode on the ear)
3, 4) right and left central leads
5, 6) right and left temporal leads
7, 8) right and left occipital leads
9, 10) right and left fronto-central bipolar EEG leads
11, 12) right and left central occipital bipolar EEG leads
13, 15) right and left fronto-mastoidal REG leads
14, 16) right and left occipito-mastoidal REG leads
17) EKG (first standard lead)

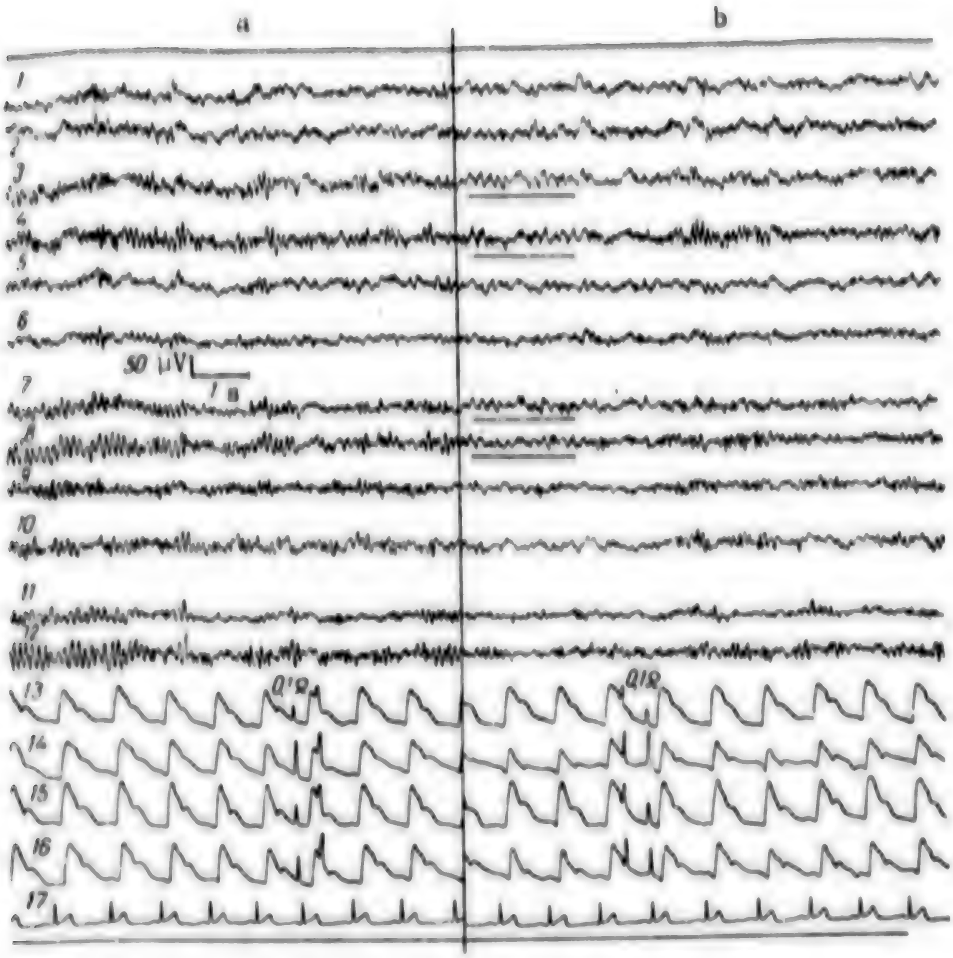

Figure 3. EEG and REG of subject M., 37 years old, with early signs of cervical osteochondrosis, before (a) and while (b) throwing the head back. While throwing the head back there is a significant decrease in maximum amplitude of the right and left occipitomastoidal REG (decreased pulsed delivery of blood to the vertebral and basilar arteries), appearance of groups of low-amplitude, polymorphic slow waves (underlined), against the background of decreased amplitude, index and slowing of main rhythm

Since ischemic reactions appear on the EEG of individuals with early signs of cervical osteochondrosis only when the supply of blood comes close to a critical level [4, 6, 7, 9, 17], a decrease in pulsed delivery of blood to the basin of the vertebral and basilar arteries to less than 30% of the base level on the side of the head turn and when it is thrown back, against the background of appearance of slow EEG activity, can be considered an important criterion of latent circulatory insufficient of the vertebral and basilar system.

Thus, synchronous recording of the REG and EEG during functional tests involving head turning and throwing the head back before and during the effect of nitroglycerin has acquired importance for expert certification, since it permits not only determination of the state of cerebral hemodynamics, but detection of latent circulatory insufficiency in the vertebrobasilar system in individuals with early signs of osteochondrosis of the cervical spine.

BIBLIOGRAPHY

1. Yarullin, Kh. Kh. in "Klinicheskaya neyrofiziologiya" [Clinical Neurophysiology], Leningrad, 1972, pp 544-559.

2. Shmidt, Ye. V. ZH. NEVROPATOL. I PSIKHIATR. [Journal of Neuropathology and Psychiatry], No 12, 1973, pp 1761-1771.

3. Vereshchagin, N. V. in "Sosudistyye zabolevaniya nervnoy sistemy" [Vascular Disease of the Nervous System], edited by Ye. V. Shmidt, Moscow, 1975, pp 398-416.

4. Boismare, F., and Boquet, J. SEM. HOP. PARIS, Vol 50, 1974, pp 819-825.

5. Kunert, W. Z. KREISL.-FORSCH., Vol 50, 1961, pp 572-580.

6. Yarullin, Kh. Kh. "Clinical Rheoencephalography," Leningrad, 1967.

7. Chukhrova, V. A. "Functional Electroencephalography in the Presence of Lesions to Great Vessels of the Head," Moscow, 1973.

8. Eninya, G. I. "Rheography as a Technique for Assessing Cerebral Circulation," Riga, 1973.

9. Ginzburg, S. Ye. "Electrical Activity and Hemodynamics of the Brain With Occlusion of Cerebral Arteries," Minsk, 1974.

10. Lebedeva, L. I. in "Metody klinicheskoy neyrofiziologii" [Methods of Clinical Neurophysiology], Leningrad, 1977, pp 40-66.

11. Alekseyev, D. A. "Regional Hemodynamics With the Use of Different Intensities of Antiorthostatic Factors," author abstract of candidatorial dissertation, Moscow, 1974.

12. Yarullin, Kh. Kh., and Tabeyeva, D. M. in "Aktual'nyye voprosy nevropatologii" [Pressing Problems of Neuropathology], Alma-Ata, 1971, pp 54-56.

13. Brotman, M. K. in "Osteokhondroz pozvonochnika" [Osteochondrosis of the Spine], Novokuznetsk, Pt 1, 1973, pp 15-22.

14. Nagulic, J., et al. VOJNOSANIT. PREGL., Vol 32, 1975, pp 8-14.

15. Konradi, G. P. "Regulation of Vascular Tonus," Leningrad, 1973, p 177.

16. Zimmer, R.; Lang, R.; and Oberdorster, G. PFLUG. ARCH. GES. PHYSIOL., Vol 328, 1971, pp 332-343.

17. Ingvar, D. H.; Sjolund, B.; and Ardo, A. ELECTROENCEPH. CLIN. NEUROPHYSIOL., Vol 41, 1976, pp 268-276.

UDC: 616.14-005.741.9-073.432.19

ULTRASONIC METHOD OF RECORDING GAS BUBBLES IN ANIMAL VENOUS BLOOD IN A RAREFIED ATMOSPHERE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 74-76

[Article by R. T. Kazakova, submitted 15 May 78]

[Text] Since 1968, there have been descriptions published of a method of recording [demonstrating] intravascular gas bubbles, which appeared under the influence of decompression due to elevated pressure, with the use of ultrasonic equipment [1-4]. With this method, it was possible to determine that the presence of gas bubbles in blood is not necessarily associated with clinical symptoms, and that bubbles may appear long before external manifestation of caisson disease. It was also established that bubbles first appear in the venae cavae, then in the aorta and pulmonary artery. As can be seen from a study conducted on dogs [5], the method of ultrasonic detection of gas bubbles permits demonstration of early stages of caisson disease and the opportunity to prevent severe forms of this disease when returning from a high ambient pressure. The authors report that with the development of appropriate sensors one can observe the process of appearance and growth of gas bubbles and, consequently, control submersion of divers and their return from deep waters. The possibility of detecting not only bubbles, but accumulations of erythrocytes, thrombocytes and fat cells, as factors related to the etiology of caisson disease, has been mentioned in several works [6, 7].

Our objective here was to test the possibility of using the ultrasonic method for detection of gas bubbles in the blood of different animals in a rarefied atmosphere.

Methods

We used an ultrasonic instrument made to our order by the Vil'nyus Scientific Research Institute of Radio Measuring Instruments to record gas bubbles in venous blood of animals. The operating principle of this instrument (Figure 1) is based on the Doppler effect. We used an ultrasonic frequency of 10 MHz. The cuff-type sensor consists of two barium titanate crystals soldered in plexiglas parallel to one another (Figure 2).

Figure 1.
Ultrasonic instrument

Figure 2. Ultrasonic sensors

In preliminary in vitro experiments, the sensor was connected to a polyvinyl chloride tube, through which we first passed tap water, then the same water but with bubbles injected with a syringe, and finally gassed water. The signals from the bubbles were heard through earphones and recorded on an electroencephalograph. In the in vivo experiments, anesthetized animals (rabbits and cats) were immobilized on a special table [stand]. We then exposed their abdominal cavity and secured the sensor on the surface of the posterior vena cava. The resulting Doppler signal

was delivered to the electroencephalograph, with concurrent use of an oscillograph and telephone. The blood flow and respiration rate were recorded continuously during the entire experiment. The animals were "lifted" to "altitudes" of 12,000-14,000 m at the rate of 150 m/s in a Votsch-2 type oxygen chamber, where they remained for 40 min. After the experiment, the animals were dissected for a thorough examination of all blood vessels and the heart. In all, we conducted 45 experiments.

Results and Discussion

In the preliminary in vitro experiments with intravenous injection of air to rabbits we became convinced that the Doppler frequency signals change in amplitude and frequency upon appearance of gas bubbles in the liquid examined. When cats were "lifted" to an "altitude" of 12,000 m, we failed to demonstrate bubbles in any of the 10 experiments. They first appeared only at an "altitude" of 14,000 m, but bubbles were found in only 1 pregnant cat out of 14 experiments, in the 2d min at that "altitude" (Figure 3). As for rabbits, it was much easier for the gas-forming process to occur in them. Thus, in 5 cases out of 14 "ascents" to an "altitude" of 12,000 m, we demonstrated bubbles in venous blood of rabbits (Figure 4), whereas in the case of "climbs" to 14,000 m, gas bubbles were present in 4 cases out of 7. As a rule, the bubbles appeared in the first 20 min at the indicated "altitude." At the postmortem, bubbles were encountered in the femoral veins, subclavian veins of the abdominal wall, posterior vena cava and pulmonary vein.

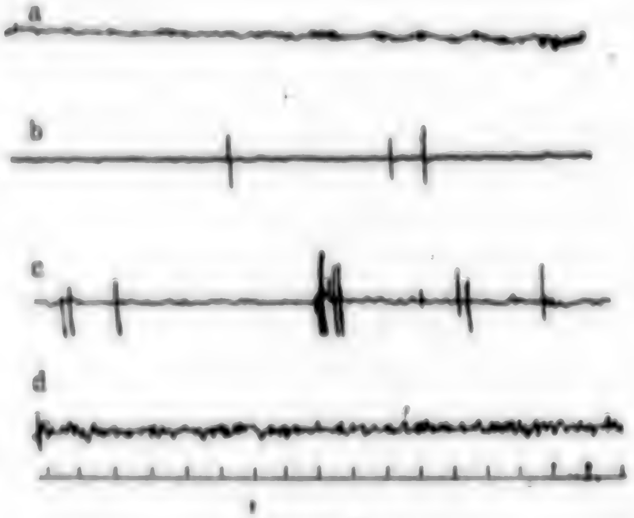

Figure 3.
Doppler signals from bubbles in a cat at an "altitude" of 13,000 m.
- a) background blood flow
- b) isolated Doppler signals in 2d min at 14,000 m
- c) numerous signals from bubbles in the 5th min
- d) absence of bubbles when animals returned to normal atmospheric pressure

Consequently, using the ultrasonic method we observed appearance of bubbles in animals in a significantly rarefied atmosphere. Our data are not in contradiction with the results of another study [8], where bubbles were visually demonstrable through an illuminator in the posterior vena cava at "altitudes" of at least 13,000 m. In our experiments, there was distinct demonstration of species-specific differences between animals, with

respect to predisposition for gas production. In rabbits, bubbles appeared in venous blood with less rarefaction than in cats ($P<0.01$ and $P<0.02$ for "altitudes" of 12,000 and 14,000 m, respectively). We cannot rule out the possibility that differences in relative blood flow rate, physicochemical and morphological properties of blood have an influence on species-specific resistance to decompression disturbances.

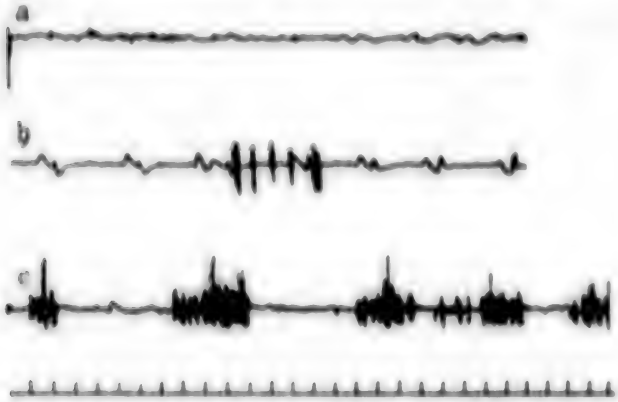

Figure 4.
Doppler signals from bubbles in rabbits at an "altitude" of 12,000 m

a) background blood flow
b) Doppler signal from bubbles in 4th min at this "altitude"
c) massive gas production; respiratory arrest

Thus, we have demonstrated the basic possibility of using the ultrasonic method to study the process of gas production in animals and man (with the use of special sensors) in a rarefied atmosphere. The feasibility of early detection of the moment of formation of gas bubbles in the body is very important in solving the problem of preventing decompression disorders. This method can be used in the system for monitoring the physiological condition of man at high altitudes.

BIBLIOGRAPHY

1. Smith, K., and Spencer, M. P. AEROSPACE MED., Vol 41, 1970, pp 1396-1400.

2. Gillis, M. F.; Karagianes, M. T.; and Peterson, P. U. SCIENCE, Vol 161, 1968, pp 579-580.

3. Powell, M. R. AEROSPACE MED., Vol 43, 1972, pp 168-172.

4. Rubissow, L. G., and Mackay, R. S. ULTRASONICS, Vol 2, 1971, pp 225-234.

5. Sapov, I. A.; Volkov, L. K.; Men'shikov, V. V.; et al. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 222, No 2, 1975, pp 508-511.

6. Nishi, R., and Livingstone, S. D. AEROSPACE MED., Vol 44, 1973, pp 179-183.

7. Philp, R. B.; Inwood, M. J.; and Warren, B. A. Ibid, Vol 43, 1972, pp 946-953.

8. Harvey, E. N. "Animal Experiments on Bubble Formation. Pt 1. Bubble Formation in Cats. Decompression Sickness," Philadelphia, 1951, pp 115-146.

UDC: 543.544.25:613.693

ISOLATION AND GAS CHROMATOGRAPHIC DEMONSTRATION OF VOLATILE ORGANIC SUBSTANCES IN THIN-LAYER BIOLOGICAL SAMPLES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 77-79

[Article by N. F. Sopikov and A. I. Gorshunova, submitted 26 Jun 78]

[Text] In addition to chemical analytical methods, modern gas chromatographic methods are used to demonstrate organic compounds in studies of the effects of space flight factors and conditions (for example, hypokinesia, radiation, hypoxia, etc.) on processes of accumulation, distribution and elimination of volatile chemicals from the human and animal organism [1-6]. At the same time, the practical use of gas chromatography is related to a number of difficulties, due to the complexity, many stages and laboriousness of the process of isolating volatile chemicals from biological media and tissues [7-10].

Our objective was to develop a simple and rapid method for isolating volatile organic substances from biological media and tissues to be submitted to gas chromatographic analysis.

This method was based on the principle of direct thermal evaporation of volatile compounds from thin-layer biological samples, obtained by using a pyrolytic attachment with the chromatograph.

Volatile substances in blood and various animal tissues were demonstrated on a chromatograph with a flame-ionization detector. We selected the absorbent for the chromatographic column, its size and temperature in accordance with the composition and physicochemical properties of the volatile substances to be analyzed in biological samples. For example, for demonstration of 1,4-dioxane in blood and various animal tissues, we used a chromatography column 2.6 m in length and with an inside diameter of 3 mm filled with celite 545 [diatomaceous earth] (granulation 0.177-0.25 mm) with 15% polyethylene glycol 2000. The chromatographic column was incubated at a temperature of 75°C. Helium was used as the gas carrier. The flow rate for helium and hydrogen constituted 30 mℓ/min and air velocity was 300 mℓ/min. The temperature of the detector and unit for input of the gas sample was 150°C.

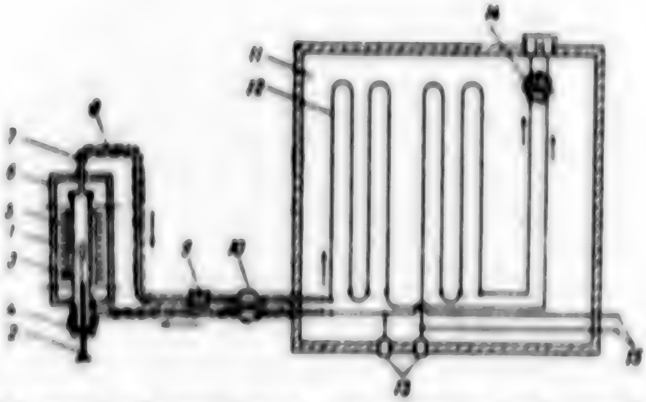

Figure 1. Diagram of pyrolytic attachment and gas lines of chromatograph

1) platinum boat
2) plunger
3) quartz tube
4) sealing coupling
5) electric heating coil
6) heater
7) connective capillary tube
8) heat-insulating sheath that is heated electrically
9) filter
10) four-way valve
11) thermostat chamber
12) chromatographic columns
13) unit for input of gas samples
14) detector
15) gas lines to tank with helium

Figure 1 illustrates the main units and system for connecting the gas lines of a tubular type attachment to the chromatograph.

In view of the high sensitivity of the flame-ionization detector of the chromatograph, we used milligram batches of biological samples. Blood, urine or organ tissue samples weighing 3 to 10 mg (usually 4-5 mg) were applied with an eye scalpel to pieces of tracing paper (10×4 mm^2, 2 mg) used as a backing, rapidly weighed on a type VT torsion balance accurate to 0.05 mg, then placed in the platinum boat *1* connected to plunger *2*, and immediately put in the unheated part of quartz tube *3*, which was sealed by turning coupling *4*, then the sample was moved with the sealed plunger into the region of the tube with a temperature of 120°C. All these operations required no more than 1 min, which reduced to a minimum any possible loss of analyzed substance due to evaporation during the process of preparing the biological sample for analysis. The use of a backing made of tracing paper ruled out direct contact between the biological sample and the boat of the pyrolytic attachment, and did not cause it to become contaminated.

We chose ordinary ["natural"] GOST 892-70 tracing paper as the most suitable material for the backing; it did not soften when wet, did not absorb substance and, at temperatures of up to 160°C, it did not discharge any

impurities that would contaminate the sample. The use of such tracing paper did not affect the results of analysis, as confirmed by the same results from demonstration of standard aqueous solutions of the substances studied which were fed into the pyrolytic cell (on the backing and without it) directly in the platinum boat.

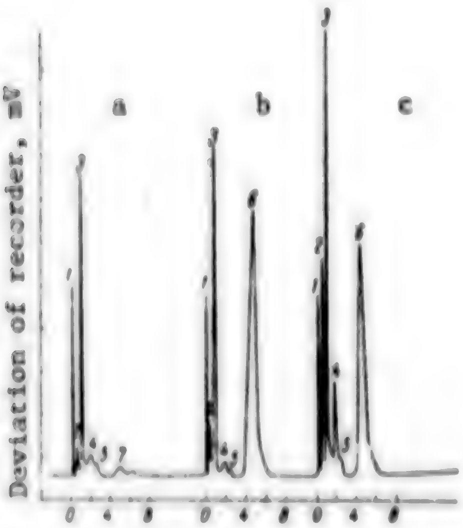

Figure 2.
Chromatogram of blood before giving dioxane (a), blood (b) and liver (c) after giving 250 mg/kg dioxane intraperitoneally
1) air
2) acetaldehyde
3) acetone
4,5) unidentified substances
6) dioxane
7) water

We found that it was sufficient to keep the biological sample in quartz tube *3* 5 mℓ in size for 2 min at 120°C to isolate organic compounds from it. Under such conditions, the sample was dehydrated, and there was denaturation of the tissue proteins it contained.

After exposure for 2 min, the discharged substances were fed through four-way valve *10* into the flow of gas carrier, through connecting capillary tube *7* and filter *9* to chromatographic column *12* for dilution, and then into the flame-ionization detector *14*.

In the gas chromatographic analysis, of biological samples, the discharged substances were recorded in the form of sharp and symmetrical peaks on the chromatogram. There was also a small and diffuse peak for water, which did not hinder detection of the analyzed substances and did not affect sensitivity of the detector (Figure 2). Concurrently, in addition to the peak for the compound administered, all chromatograms recorded the peaks for a number of endogenous substances that are formed during natural metabolism in tissues. The substances consistently demonstrable, which are released in significant quantities from different tissues, blood and urine, include, in particular, methane, ethanol, acetone, acetaldehyde and others, the concentrations of which reached 0.5–2.5 mg%.

We chose 1,4-dioxane, which has relatively low volatility (135 mg/ℓ), low rate of transformation and tissues and is well soluble in liquid biological media, to assess the accuracy of the analytical method.

In the experiments involving examination of blood, into which we first injected 1,4-dioxane in an estimated concentration of 0.2 μg/10 μℓ, we established that the results of gas chromatographic assay of dioxane in blood samples differed from assays of this substance in a standard aqueous solution, as well as from the estimated level, by only 2-5%, which was within the range of reading error. Repeated analysis of remainders of blood samples that previously contained 0.2 μg dioxane failed to demonstrate the latter, which was indicative of complete elimination thereof. Analogous findings were made in assaying dioxane content of tissues.

Rat brain and liver homogenates were prepared for quantitative assays of dioxane in tissues. Batches of tissues, each weighing 2.0 g, were put in 5-mℓ weighing bottles, into which we decanted different amounts of aqeueous dioxane solution containing 200 μg substance per mℓ, and mixed thoroughly. Concurrently, various amounts of standard dioxane solution were decanted into weighing bottles with 2.0 mℓ water. The results of analysis of 3-mg (4-5 mg) samples of tissue homogenates and water containing different concentrations of dioxane are listed in the Table.

Assays of dioxane in tissue homogenates and water (M±m)

Size of sample μg/g/mℓ	Dioxane demonstrated, μg/g		
	brain	liver	water
9.6	10,2±0,4	9,4±0,3	10,4±0,4
26.0	26.6±0.8	25.0±1.0	26.0±0.6
40.0	40.5±1.8	38.8±1.3	39.5±1.5
66.6	68,7±1,9	65,7±1,7	67,5±2,8
100,0	102,0±3,0	100,2±3,3	102,1±3,5

The data listed in this table indicate that there is good coincidence of results of analyzing dioxane in tissue homogenates and water. The error of assays, as compared to estimated levels, did not usually exceed 3-5%, and reached 11-12% in only a few cases with lower concentration of dioxane (9.6 μg/g).

It must be noted that the proposed method for analysis of organic substances permits assay thereof not only in homogenates requiring large tissue samples, but directly in thin-layer milligram samples. For this purpose, thin-layer sections were prepared from the liver of rats previously given dioxane, dichloroethane and other compounds; these sections were then placed on a backing of tracing paper, weighed and analyzed by the method described above. As a control, we assayed these substances in homogenates of tissue taken from the same region of the liver

and applied to tracing paper in a thin layer. The difference between the results of analysis of sections and homogenates of the liver did not exceed 10%, which is within the range of error of the method.

Our data are indicative of the validity of using thin-layer sections instead of homogenates of tissues, and this has several advantages, particularly when studying the process of distribution of substances in the body. The simple and rapid preparation of biological samples reduces to a minimum any possible loss of volatile compounds. The small tissue samples (3-10 mg) permit examination of structures with low weight (adrenals, pituitary, etc.). It also permits, in particular, the study of distribution of chemicals in different parts of the central nervous system of small laboratory animals, such as mice and rats.

Thus, after intravenous injection of 1,2-dioxane in a dosage of 50 mg/kg, we demonstrated the following amounts (in mg%): 0.8 in the cerebral cortex, 0.93 in the thalamus, 0.66 in the hypothalamic region, 0.89 in the caudate nucleus, 0.6 in the hypophysis, 0.94 in the cerebellum, 1.2 in the lamina quadrigemina, 1.60 in the medulla oblongata and 2.65 in the spinal cord.

Thus, the proposed method is notably universal: it permits demonstration in the same biological sample of volatile organic substances, not only of exogenous, but endogenous origin; under identical (standard) conditions, it permits analysis of both liquid biological media (blood, urine) and various tissues and organs, which increases the reliability of results of comparative studies of distribution of chemicals in the body with exposure to various habitat factors.

The minimum demonstrable amounts of substances are in the range of 0.01 to 0.02 μg in the biological sample.

This simple and rapid micromethod for assaying volatile organic substances in biological media can be used in toxicological and hygienic studies for scientific diagnostic purposes in cases of acute and subacute poisoning.

BIBLIOGRAPHY

1. Bugar', K. P.; Kustov, V. V.; Abidin, V. I.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1977, pp 83-84.

2. Kustov, V. V.; Abidin, B. I.; Belkin, V. I.; et al. Ibid, No 1, 1976, pp 70-73.

3. Nefedov, Yu. G.; Zaloguyev, S. N.; and Savina, V. P. Ibid, No 2, pp 30-34.

4. Savina, V. P.; Sokolov, N. L.; and Nikitin, Ye. I. Ibid, No 6, pp 62-66.

5. Sokolov, N. L. "Studies of Composition of Microimpurities in Air Exhaled by Man and Their Role in Pollution of the Air Environment of Hermetically Sealed Rooms," author abstract of candidatorial dissertation, Moscow, 1972.

6. Tiunov, L. A.; Kolosova, T. S.; Lazurenko, D. T.; et al. KOSMICHESKAYA BIOL., No 1, 1976, pp 61-65.

7. Mikulin, S. G.; Kurchatov, G. V.; and Kofanov, V. I. in "Farmakologiya i toksikologiya" [Pharmacology and Toxicology], Kiev, Vyp 10, 1975, pp 162-164.

8. Murav'yeva, S. I.; Osipenko, N. I.; and Gubina, N. B. GIG. TRUDA [Industrial Hygiene], No 7, 1974, pp 31-34.

9. Yavorovskaya, S. F., and Gubina, N. B. GIG. I SAN. [Hygiene and Sanitation], No 12, 1971, pp 61-68.

10. Iffland, R., and Dotzauer, G. ARZNEIMITTLEFORSCH., Vol 17, 1967, p 918.

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A STAND FOR SIMULATION OF PHYSIOLOGICAL EFFECTS OF WEIGHTLESSNESS IN LABORATORY EXPERIMENTS ON RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 79-80

[Article by Ye. A. Il'in and V. Ye. Novikov, submitted 26 Jan 79]

[Text] We were governed by the following requirements in developing the stand for simulation of physiological effects of weightlessness in laboratory experiments on rats: provide for increased blood supply to the head part of the trunk; reduce to a minimum the influence of such undesirable incidental factors as immobilization and restriction of movement; eliminate entirely the weight load on the hind limbs with partially reduced load on the front ones, that the animal could use to move about, independently take in feed and water.

The stand consists of a frame, on which a beam with movable carrier can move over two guide rails (see Figure). The carrier can move in any direction in the horizontal plane above wire flooring 40×40 cm in size, under which a tray is placed to collect excrements. A special system is used, which consists of a capron [nylon-6] rat suit with openings for the limbs and a wire frame, to suspend the animal on the carrier, in order to obtain uniform distribution of the weight load on the trunk.

The animal is suspended in such a manner as to totally eliminate any weight load on the hind legs by partially lifting the entire animal in a tilted position, the the head end down. Such suspension partially removes the weight load on the rat's forelegs and, in addition, creates conditions for increased supply of blood to the head end of the trunk. The animal can move about freely using its front legs over the wire flooring of the stand, in any direction, it can come up on its own to the feeder and water container, and use them. As shown by tests on this stand, retention of mobility has a favorable effect on the animal's general condition; it also eliminates restlessness and aggressiveness, which are inherent in the first days of experiments under hypokinetic conditions.

General view of stand; described in the text

Morey proposed an analogous principle for modeling the physiological effects of weightlessness in laboratory experiments on rats [1]. However, the design of the stand and, particularly, the suspension system differ from what we have described above. According to Morey, comparative analysis of the findings in rats that had spent the same length of time aboard Cosmos biosatellites and in suspended position on the stand revealed identical changes in bones of the limbs and rate of weight gain. All this means that the proposed method can be used with success for laboratory studies of mechanisms of some physiological reactions that occur in animals under weightless conditions.

BIBLIOGRAPHY

1. Morey, E. BIOSCIENCE, Vol 29, 1979, pp 168-172.

BRIEF REPORTS

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GLYCOPROTEIN CONTENT OF HUMAN BONE TISSUE AFTER SPACE FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 81-82

[Article by A. A. Prokhonchukov and V. K. Leont'yev, submitted 10 Oct 78]

[Text] The state of calcium metabolism in the body during exposure to space flight factors and, chiefly, weightlessness is one of the pressing problems of space biology and medicine. In spite of the fact that some advances have been made in the study thereof, this problem remains unclear and debatable in many respects [1].

The main factor of dynamic stability of the mineral fraction of osseous tissue (chiefly calcium) is the close correlation between minerals and the organic fraction of osseous tissue, most of which consists of collagen and noncollagen proteins, and glucosamine glycans. Noncollagen proteins of mineralized tissues constitute a little-studied group of glycoproteins of connective tissue, the carbohydrate part of which is chemically bound with the protein part and consists of fucose, neuraminic acid, hexosamines and other sugars [2-5]. They are the most active proteins of connective tissue, as indicated by their involvement in fibril formation, aggregation of collagen fibers and their primary fixation of calcium [6-9]. Studies have shown that each type of mineralized tissue, in particular bone as an organ, is characterized by its own set of protein-bound carbohydrates. The glycoproteins determine the species-specific, functional and age-related distinctions of bone tissue. Glycoproteins play an important role in processes of formation and regeneration of collagen fibers [4, 8, 10]. There have been descriptions of impairment of their metabolism in the presence of bone pathology [4, 11].

Glucosamine glycans are involved in the transport and binding of fluid and inorganic ions in bone tissue [3, 4]. Changes in levels thereof have been demonstrated in experiments with hypokinetic rats [12].

Thus, glycoproteins and glucosamine glycans of osseous tissue are among the important elements of its homeostasis, related to the mineral and organic phases of bone, mechanism of fixation of calcium, most of which is contained in hydroxyapatite. Glycoproteins provide for the main mechanical

qualities of bone, namely its plastic properties: resistance to flexing, torsion, stretching and compression loads.

Our objective included the study of glycoprotein content of the organic fraction of human bone tissue after a space flight (autopsy material from the crew of Salyut-1 orbital space station).

Methods

We used samples of osseous tissue from the calcaneus for our study [1]. This bone is subject to the main orthostatic and dynamic load, and it reacts sensitively to changes in gravity.

We used tissue from the calcaneus obtained from atuopsies on three men who died of acute trauma at the age of 20-40 years (without patho-anatomically demonstrable signs of diseases of viscera and systems) as a control for comparative analysis.

We treated the bones with proteolytic solution for complete removal of soft tissues [13]. Glycoprotein and glucosamine glycan content was assayed according to the quantity of protein-bound hexosamines, hexoses, fucoses, uronic and neuraminic acids and ketoses (in mg% dry bone weight, using the method described previously [14]). The digital data were submitted to statistical processing.

Results and Discussion

We demonstrated in all bone samples examined appreciable amounts of protein-bound carbohydrates: total hexoses, ketose, fucose, uronic and sialic acids, and hexosamines. This shows that, in addition to collagen protein, there were significant amounts of glycoproteins and glucosamine glycans in the bone tissue examined. The quantitative composition of glycoproteins of osseous tissue that we obtained coincides with data in the literature [2-4, 14, 15].

Comparative analysis of protein-bound carbohydrates in the test and control groups revealed that there was no statistically reliable difference in levels of most of the bone tissue components studied (see Table). We demonstrated a 23.5% decrease in uronic acid content and 19.5% increase in hexosamines of bone tissue in the tested group, as compared to the control; however, these differences were statistically unreliable (see Table). A comparison of our assays of glycoprotein content of bone tissue to data in the literature [2, 11, 14], including those related to diverse bone pathology [4, 14, 15], warrants the belief that the demonstrated changes in levels of different components of glycoproteins (uronic acids, ketoses) do not justify interpretation thereof as signs of bone pathology. Thus, we failed to demonstrate consistent deviations of composition of glycoproteins of human bone tissue after a space flight.

Glycoprotein content (mg%) of osseous tissue (M±m)

Glycoproteins	Group	
	control	test
Hexoses	1047,0±55,0	1013,0±27,0
Hexosamines	226,0±67,0	270,0±6,0
Sialic acids	26,3±2,4	23,7±1,4
Ketoses	65,0±12,0	67,0±4,0
Fucose	111,0±12,0	102,0±13,0
Uronic acids	213,0±34,0	163,0±32,0

On the basis of analysis of the literature and the results of these studies, it may be assumed that the findings confirm the previously expounded hypothesis, to the effect that the normal state of bone tissue after space flights is attributable to the high level of physical conditioning of cosmonauts and subsequent use, aboard the Salyut-1 orbital space station, of the set of equipment and conditioning measures to rule out the undesirable effects of space flight factors on the human body [1, 16, 17].

BIBLIOGRAPHY

1. Gazenko, O. G.; Prokhonchukov, A. A.; Panikarovskiy, V. V.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1977, pp 11-20.

2. Bourne, G. H. (editor) "The Biochemistry and Physiology of Bone," New York, Vol 1-3, 1971.

3. Vaughan, J. M. "The Physiology of Bone," Oxford, 1975.

4. Slutskiy, L. I. "Biochemistry of Normal and Pathologically Altered Connective Tissue," Leningrad, 1969.

5. Torbenko, V. P., and Kasavina, B. S. "Functional Biochemistry of Bone," Moscow, 1977.

6. Herring, J. M. BIOCHEM. J., Vol 159, 1976, pp 749-755.

7. Franzblan, C.; Schmidt, K.; Faris, B.; et al. BIOCHIM. BIOPHYS. ACTA, Vol 427, 1976, pp 302-314.

8. Leont'yev, V. K. in "Belki i fermenty v klinicheskikh i eksperimental'nykh issledovaniyakh" [Clinical and Experimental Studies of Proteins and Enzymes], Omsk, 1977, pp 44-46.

9. Leont'yev, V. K.; Desyatnichenko, K. S.; and Levchenko, L. T. Ibid, pp 46-49.

10. Kasavina, B. S., and Zenkevich, G. D. BIOKHIMIYA [Biochemistry], Vol 25, 1960, pp 669-672.

11. Casuccio, C. J. BONE JT. SURG., Vol 44B, 1962, pp 453-459.

12. Potapov, P. P. KOSMICHESKAYA BIOL., No 3, 1977, pp 44-48.

13. Gaydamak, A. N., and Leont'yev, V. K. in "Eksperimental'naya i klinicheskaya stomatologiya" [Experimental and Clinical Stomatology], Moscow, Vol 6, 1975, pp 46-49.

14. Leont'yev, V. K., and Gaydamak, A. N. LABOR. DELO [Laboratory Record], No 5, 1978, pp 290-293.

15. Prokhonchukov, A. A.; Zhizhina, N. A.; Leont'yev, V. K.; et al. in "Etiologiya i patogenez osnovnykh stomatologicheskikh zabolevaniy" [Etiology and Pathogenesis of the Main Stomatological Diseases], Moscow, 1977, pp 54-57.

16. Vasil'yev, P. V. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 278-297.

17. Stepantsov, V. I.; Yeremin, A. V.; and Tikhonov, M. A. Ibid, pp 298-313.

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VEGETOPOSTURAL REACTIONS IN ANTIORTHOSTATIC POSITION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 82-84

[Article by K. L. Geykhman and M. R. Mogendovich, submitted 30 Oct 78]

[Text] Much significance is attributed to the antiorthostatic [head down] position (AOP) in simulating the physiological effects of weightlessness. This refers to the body's position in space that is opposite to orthostatic position.

Orthostasis is the usual state, which developed in phylogenesis and ontogenesis, and AOP elicits an extreme and biologically unstable state. It is not inherent in man, and it is often on the borderline of pathology.

Let us first discuss complete AOP (CAOP), i.e., vertical position with the head down. We tested the cardiovascular system, external respiration, motility in the initial (orthostatic) position, then during 1-min AOP and in the aftereffect period (return to orthostatic position). We had the following objectives: to determine how human physiological functions change; to trace the compensatory mechanisms of the body to normalize circulation in this position (homeostasis); to determine whether it is possible for these mechanisms to adjust by means of conditioning. We studied the changes in the autonomic nervous system by means of arterial oscillography, electrocardiography, pulsotachometry, cutaneous thermometry and oxyhemography. Concurrently, we measured the tonus of skeletal muscles with an electromyotonometer, and determined the latency period of motor reactions of the arms and legs to an exogenous signal [1, 2].

Our results revealed that the change from orthostatic position to CAOP is associated with drastic changes in activity of the cardiovascular system, oxygenation of blood and motility. CAOP is characterized by the following physiological changes: slowing of heart rate by a mean of 7.8/min in passive CAOP and by 2.3 in active CAOP' elevation of maximum and drop of diastolic pressure, elevation of oscillatory index and minor change in mean pressure in passive AOP; elevation of temperature of the skin on the forehead by 0.7°C in active position and 0.3°C in passive; 7.6% decrease in blood oxygenation. The changes in the autonomic nervous system were associated with drastic

increase in tonus of arm muscles, some tonic tension of the legs in the active position, as well as longer latency period of the motor reactions of arms and legs.

Studies of athletes involved in different sports revealed that regular practice of special physical exercises improves reflex mechanisms that counteract gravity. The body adjusts to unusual positions, as a result of which there is attenuation of disturbances of the autonomic nervous system [3].

A set of adaptational and compensatory neurohumoral mechanisms are involved in normalization of the gravitational changes in blood in CAOP. Of basic importance is determination of the mechanism of postural and vegetative reflexes, which regulates the functional state of the cardiovascular system in CAOP by means of proprioceptive impulsation.

We studied postural and vegetative reflexes not only in CAOP, but with small angles of inclination, produced by using a special turntable or chair.

Data pertaining to passive AOP with a tilt angle of 30° were submitted in the work by G. Z. Chuvayeva [4, 5]. M. D. Berg reported the hemodynamic parameters of school children 7-8 and 14-16 years of age in the same position [6, 7]. V. A. Shchurov used passive AOP at an angle of 30° [8] and S. N. Khmeleva used angles of 30 and 45° [9]. Their findings confirm the existence of a correlation between postural tonus of skeletal muscles and condition of vessels (motor-vascular reflex).

Later on, R. M. Bayevskiy used AOP with 15 and 30° angles [10]. Studies involving the use of long-term hypokinesia [11, 12] revealed that AOP with a tilt angle of -4° is more demonstrative than the horizontal position. AOP with angles of -4, -8, -12, -16 and -20° was used by other authors also [13-15]. At the suggestion of M. R. Mogendovich, in addition to ordinary AOP (with the legs straight), a special AOP with the legs elevated and bent at the knees was used. This position was named "position No 2." This position is a more effective model of redistribution of blood in weightlessness than position No 1 [15-19]. Underestimation of the leg position in AOP could lead to misinterpretation of minute volume and other hemodynamic parameters. A combination of AOP and prolonged hypokinesia yields particularly rich information.

Further studies are needed for use of data obtained in tests with AOP in screening cosmonauts and developing preventive measures [20].

BIBLIOGRAPHY

1. Geykhman, K. L. "The Most Important Vegetative Changes in Man in Antiorthostatic Position," candidatorial dissertation, Perm', 1965.

2. Geykhman, K. L., and Zuyev, R. V. in "Nauchno-prakticheskaya konf. po fizicheskomy vospitaniyu, fiziologii sporta, vrachebnomu kontrolyu i lechebnoy fizicheskoy kul'ture. 2-ya. Materialy" [Proceedings of 2d Scientific and Practical Conference on Physical Education, Physiology of Sprots, Medical Monitoring and Therapeutic Physical Culture], Perm', 1967, pp 64-66.

3. Alekseyev, D. A.; Yarullin, Kh. Kh.; Krupina, T. N.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1974, pp 66-72.

4. Chuvayeva, G. Z. in "Motorno-vistseral'nyye i pozno-vegetativnyye refleksy" [Visceromotor and Vegetopostural Reflexes], Perm', 1965, pp 54-58.

5. Chuvayeva, G. Z. in "Novoye v fiziologii i patologii motorno-vistseral'nykh refleksov" [News in Physiology and Pathology of Visceromotor Reflexes], Perm', 1967, pp 42-46.

6. Berg, M. D. in "Motorno-vistseral'nyye i pozno-vegetativnyye refleksy," Perm', 1965, pp 59-65.

7. Berg, M. D. "Age-Related Aspect of Vegetopostural Reflexes of the Cardiovascular System," candidatorial dissertation, Perm', 1967.

8. Shchurov, V. A. "Functional Studies of Age-Related Distinctions in Delivery of Blood to the Human Limbs," candidatorial dissertation, Perm', 1969.

9. Khmeleva, S. N. in "Voprosy fizicheskoy kul'tury i sovershenstvovaniye uchebnogo protsessa" [Problems of Physical Culture and Refinement of the Learning Process], Volgograd, Vyp 1, 1969, pp 245-247.

10. Bayevskiy, R. M. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 6, 1972, pp 819-827.

11. Genin, A. M., and Kakurin, L. I. KOSMICHESKAYA BIOL., No 4, 1972, pp 26-28.

12. Pometov, Yu. D., and Katkovskiy, B. S. Ibid, pp 39-46.

13. Sidorov, N. I. in "Teoriya i praktika fizicheskogo vospitaniya i sporta" [Theory and Practice of Physical Education and Sports], Perm', 1975, pp 141-142.

14. Gubman, L. B. Ibid, pp 89-90.

15. Gubman, L. B.; Komin, S. V.; and Petrov, B. V. in "Vozrastnyye osobennosti dvigatel'nykh i vegetativnykh funktsiy i ikh vzaimodeystviye pri razlichnykh vidakh myshechnoy aktivnosti" [Age-Related Distinctions of Motor and Autonomic Functions, and Interaction Thereof During Different Forms of Muscular Activity], Kalinin, 1973, pp 123-134.

16. Geykhman, K. L.; Gusev, A. N.; Degtyarev, P. G.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 2, 1975, pp 127-130.

17. Gubman, L. B., and Petrov, B. V. in "Nauchnyye osnovy fizicheskoy kul'tury" [Scientific Bases of Physical Culture], Kalinin, Vyp 2, 1974, pp 12-28.

18. Degtyarev, P. G., and Mogendovich, M. R. in "Vozrastnyye osobennosti motorno-vistseral'noy regulyatsii pri razlichnykh vidakh myshechnoy activnosti" [Age-Related Distinctions of Visceromotor Regulation During Different Types of Muscular Activity], Kalinin, Vyp 3, 1975, pp 65-66.

19. Petrov, B. V. Ibid, pp 67-76.

20. Geykhman, K. L., and Mogendovich, M. R. KOSMICHESKAYA BIOL., No 3, 1977, pp 74-75.

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USE OF CYTOCHEMICAL PARAMETERS OF PERIPHERAL BLOOD NEUTROPHILS TO STUDY HORMONAL AND ENDOCRINE REACTIONS TO FLIGHT WORK LOADS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 84-85

[Article by P. S. Pashchenko, A. V. Pastushenkov, V. V. Grishchenko and I. V. Lemak, submitted 4 May 79]

[Text] Since pilot work is related to constant emotional stress, some investigators [1-4] used methods that enabled them to study the reaction of the adrenohypophyseal system to the complex effects of flight factors: 17-hydroxycorticosteroid (17-HCC) content of urine, precipitation color reaction according to Kimbarovskiy (PCRK) and others. Elevation of corticosteroid, sugar, choleterol levels in blood, as well as 17-HCC in urine of pilots, after completing flights were usually related by authors to high levels of nervous and emotional tension. Analysis of data obtained for PCRK is difficult because of the low specificity of this reaction and its unclear chemistry [5].

Our objective was to find an adequate object and certain indicators of humoral and endocrine influences in pilots as related to different levels of flight work.

In our opinion, one should use cells of tissues that are not subject to direct neural regulation (i.e., that do not contain nerve cells), in which regulatory processes are implemented by incretory influences, as the object of investigation to isolate the hormonal-endocrine component of the general system of regulatory influences. The cellular elements of peripheral blood are adequate and accessible objects of this type. For these cells, the exogenous environment is blood plasma, in which a chain of hormonal effects develops, which induce various chemical conversions in the cells.

Flight work activates the pilot's adrenohypophyseal system, and this is associated with elevation of blood catecholamines and urine 17-HCC [1, 4], leading to a change in carbohydrate metabolism. The effect of catecholamines on carbohydrate metabolism of cells can also be studied indirectly. It is known that glycogen breaks down in cells as a result of increase in

phosphorylase activity. This enzyme changes from inactive to active form as a result of the mediated effect on it of such incretory substances as epinephrine and glucagon (there are data to the effect that their influence on carbohydrate metabolism is similar to some extent [6]. In our studies, glycogen content of neutrophil cytoplasm and activity of phosphorylase in neutrophils served as indicators of the regulatory influence of adrenalin on carbohydrate metabolism of cells.

Methods

We took blood from the finger. The PAS reaction according to McManus and Hotchkiss was run to demonstrate cytochemically cytoplasmic neutrophils. This substance was identified in control blood smears by treating them with a saliva solution for 30 min at a temperature of 37°C. Phosphorylase was demonstrated by the method of Tekeuchi [7]. We assessed glycogen content of cells on the basis of optical density of the reaction product, using the method of single-beam scanning cytophotometry with a cytophotometer designed on the order of the MUF-6 type (photographic variant) in the laboratory of histological chemistry of Voronezh Medical Institute. Optical density of the product of the cytochemical reaction was calculated with the following formula:

$$\varepsilon = \frac{1}{\log I_1 - \log I_2}$$

where ε is optical density, $\log I_1 - \log I_2$ is the logarithmic difference characterizing attenuation of the optical beam. The error factor of the method is in the range of 10% [8].

We assessed cytochemical activity of phosphorylase according to number of granules in the product of the cytochemical reaction, on the basis of the fact that the number of granules of this enzyme reflects the number of its "active centers" in cell cytoplasm. We studied 30 cells for demonstration of the substances in question in each pilot (student) under experimental conditions and in the background. The data were submitted to statistical processing with the use of Student's criterion.

We examined 10 students after 2 introductory flights and 8 pilots after 3 test flights 1.5-2 h before the flights (background) and 10-15 min after the flight shift was over (experiment). The flight work load was assumed to be insignificant for the students, unlike pilots, since they did not participate directly in piloting the aircraft (which was controlled by experienced instructors).

Results and Discussion

After two introductory flights, glycogen content of blood neutrophils did not differ reliably ($P>0.05$) from the levels demonstrated 1.5-2 h before the flights. Phosphorylase activity was also virtually the same as in the background (see Table). Thus, there is no reason to believe that humoral

and endocrine reactions had any marked influence on carbohydrate metabolism of peripheral blood cells after the students' two introductory flights.

Some cytochemical parameters of carbohydrate metabolism of peripheral blood neutrophils of pilots and students after completion of flights for different purposes

Cytochemical parameter	Flight load	Time of study	
		1.5-2 h before flight	10-15 min after flight shift
Optical density of product of cytochemical reaction for glycogen in neutrophil cytoplasm, arbitrary units ($M\pm\sigma$)	Two introductory flights (students)	22.3±8.7	20±9.0
Mean number of granules of product of cytochemical reaction for phosphorylase in neutrophil cytoplasm		8.8±3.9	9.5±2.7
Optical density of product of cytochemical reaction for glycogen in neutrophil cytoplasm, arbitrary units ($M\pm\sigma$)	Three pilotage flights (pilots)	36.0±13.7	22.5±10.1*
Mean number of granules of product of cytochemical reaction for phosphorylase in neutrophil cytoplasm		9.8±2.4	15.6±3.8

*$P<0.05$

The findings were different with regard to glycogen content and phosphorylase activity. After the flight shift (see Table), there was a reliable decrease in glycogen content of neutrophil cytoplasm (by 39%) and increase in phosphorylase activity in the pilots. This is indicative of obvious intensification of endocrine influence on blood cell chemistry, and according to current conceptions this shows intensification of incretory function of the adrenal cortex [9].

This conclusion is consistent, to some extent, to the data of other authors, who observed an increase in 17-HCC in urine after flights [3].

We became convinced that the glycogen outlay was unrelated to performance of a specific function by neutrophils by the fact that we failed to demonstrate phagocytosis in these cells, since we took material for our study from essentially healthy individuals.

Thus, the parameters of carbohydrate metabolism of blood neutrophils that we studied can serve as a sort of "mirror" of hormonal and endocrine reactions to flying work loads.

BIBLIOGRAPHY

1. Arutyunov, G. A.; Vorob'yev, N. A.; Kuznetsov, N. I.; et al. VOYEN.-MED. ZH. [Military Medical Journal], No 1, 1963, pp 60-64.

2. Diusskaya, I. G.; Kosmolinskiy, F. P.; and Fedorov, N. A. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, 1963, pp 165-169.

3. Kosmolinskiy, F. P. VOYEN.-MED. ZH., No 6, 1965, pp 63-64.

4. Idem, "Emotional Stress When Working Under Extreme Conditions," Moscow, 1976.

5. Bokunyayeva, N. I. in "Spravochnik po klinicheskim laboratornym metodam issledovaniya" [Manual of Clinical Laboratory Test Methods], Moscow, 2d edition, 1975, pp 232-233.

6. Sutherland (1956, 1959) quoted in "Vvedeniye v klinicheskuyu biokhimiyu" [Introduction Into Clinical Biochemistry], edited by I. I. Ivanov, Leningrad, 1969, p 430.

7. Lilly, R. "Pathohistological Techniques and Practical Histochemistry," edited by V. V. Portugalov, Moscow, 1969, pp 306-307.

8. Pevzner, L. Z. "Functional Biochemistry of Neuroglia," Leningrad, 1972, pp 32-33.

9. Ivanov, I. I.; Zarembskiy, R. A.; Korovkin, B. F.; et al. "Vvedeniye v klinicheskuyu biokhimiyu," Leningrad, 1969.

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EVALUATION OF THE FUNCTIONAL STATE OF THE HUMAN CARDIOVASCULAR SYSTEM DURING PROLONGED ANTIORTHOSTATIC HYPOKINESIA, USING DIFFERENT LEVELS OF PHYSICAL EXERCISE ON A BICYCLE ERGOMETER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 86-87

[Article by B. S. Katkovskiy and V. P. Buzulina, submitted 3 Feb 78]

[Text] The functional tests involving physical loads of about 400 kg-m/min during the flight aboard Salyut-4 orbital station failed to demonstrate appreciable changes in functional state of crew members [1]. At the same time, signs indicative of poorer endurance of physical work were found in all of the cosmonauts after the flights [2]. The discrepancies between flight and postflight data could be due to the fact that the postflight tests were conducted during the acute period of readjustment to earth's gravity, as well as that the test load was somewhat greater (600 kg-m/min) in the preflight and postflight tests than during the flight.

The reaction of the human body to physical work is determined by the extent and duration of such work. It is a known fact that the values of different parameters of the circulatory system at rest (particularly when one fails to adhere to the usual conditions for testing basal metabolism) may vary from test to test over a rather wide range in the same person. Emotional and other influences are not entirely eliminated with small physical work loads, and therefore the results of functional tests with a small load could also vary, thus making it difficult to demonstrate the influence of the factor under study. One generally simulates the influence of weightlessness on the cardiovascular system in the laboratory by means of ordinary bed rest or hypokinesia in antiorthostatic (ANOH) position [head tilted down] [3-5]. Unquestionably, physical exercise performed "lying down" is a more adequate model of the functional tests that the cosmonauts perform during a flight than the same exercise performed in "seated" position. For this reason, we planned to conduct tests with different levels of physical loads with the subjects in "lying down" position in the study involving prolonged ANOH (-4°).

Methods

We conducted the studies on 12 volunteer subjects who had undergon special medical screening and were deemed to be essentially healthy. After the background studies, the subjects were divided into two groups, with six people in each. We used anthropometric data, as well as indices of resistance to various (including maximum) physical loads and orthostatic tests, in order to form homogeneous groups. The first group of subjects performed a set of physical exercises developed and tested by V. A. Tishler [6], twice a day while in ANOH. The caloric value of the exercises constituted about 300 kcal/h. The second group (control) did not exercise. Before and on the 45th day of ANOH, all of the subjects performed 5-min tests with physical loads of 150, 300, 600 and 800 kg-m/min in "lying down" position. There was a 5-min interval between the first and second load, and 10-15-min between subsequent ones.

Results and Discussion

We analyzed the pulse rate recorded in the 5th min of each physical load. Our findings and data in the literature indicate that, in most cases, this is enough time for various parameters of the cardiovascular and respiratory systems to establish a " table state" [7]. As can be seen in the Table, there were insignificant intergroup differences in the background period with the different physical loads.

Pulse rate in the 5th min of tests with graduated physical loads performed "lying down" before (background) and on the 45th day of ANOH

Group	Subjects	Load (kg-m/min) and time of test											
		150			300			600			800		
		BG	45th day	Δ	BG	45th day	Δ	BG	45th day	Δ	BG	45th day	Δ
1	D-ov	101	106	+5	105	110	+5	119	123	+4	134	131	−3
	A-yev	87	91	+4	94	99	+5	110	117	+7	131	130	−1
	M-ov	83	80	−3	95	88	−7	114	108	−6	132	127	−5
	P-ov	75	83	+8	85	90	+5	100	106	+6	110	114	+4
	G-ov	92	92	0	98	95	−3	124	125	+1	129	160	+31
	G-in	99	95	−4	109	108	−1	133	134	+1	150	157	+7
2	A-ov	93	115	+22	99	125	+26	126	165	+39	154	173	+19
	P-ov	90	88	−2	98	105	+7	112	126	+14	114	141	+27
	K-ov	82	83	+1	89	95	+6	116	125	+9	128	149	+21
	F-ov	121	115	−6	123	125	+2	145	157	+12	159	174	+15
	O-ov	92	88	−4	97	100	+3	120	128	+8	140	164	+24
	Sh-ov	86	77	−9	92	83	−11	106	103	−3	112	130	+18

Note: Δ refers to difference between pulse rate on 45th day of ANOH and in the background period; BG--background.

In most subjects who worked out, the pulse reaction to physical loads only changed insignificantly under the influence of ANOH. Changes occurred in different directions, not only from person to person, but in the same subject from load to load. In only 1 case did the pulse rate increase by 31/min with a load of 800 kg-m/min. The same subject demonstrated other signs of deterioration of the functional state of the cardiovascular system: extrasystoles after loads of 600 and 800 kg-m/min.

The subjects in the second group presented substantially decreased endurance of physical exercise; however, this was distinctly demonstrable with relatively heavy physical loads. Thus, the mean group reaction of pulse rate to a load of 150 kg-m/min showed virtually no change, as compared to the background, and increased negligibly with a load of 300 kg-m/min (see Table). With a load of 800 kg-m/min, all 6 subjects showed an increase of 15-25/min in pulse rate, as compared to the background load. In 1 case, the test was stopped at the subject's request because he did not feel well. With a load of 600 kg-m/min, an increased pulse reaction was demonstrated in 5 out of the 6 subjects.

Thus, our data indicate that small physical loads are not demonstrative for evaluation of functional changes in the human cardiovascular system in studies simulating prolonged weightlessness. Evidently, even in a real space flight, the functional state of crew members should be assessed with the use of physical loads of at least 800 kg-m/min, particularly when the flight program requires significant physical exertion of the cosmonaut.

BIBLIOGRAPHY

1. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. N.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1976, pp 3-18.

2. Beregovkin, A. V.; Vodolazov, A. S.; Georgiyevskiy, V. S.; et al. Ibid, pp 24-30.

3. Genin, A. M., and Kakurin, L. I. Ibid, No 4, 1972, pp 26-28.

4. Parin, V. V., and Krupina, T. N. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii" [Adjustment to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 134-135.

5. Kakurin, L. I., and Katkovskiy, B. S. in "Fiziologiya cheloveka i zhivotnykh" [Human and Animal Physiology], Moscow, 1966, pp 6-29.

6. Kakurin, L. I.; Katkovskiy, B. S.; Timler, V. A. KOSMICHESKAYA BIOL., No 3, 1978, pp 20-27.

7. Katkovskiy, B. S. "Some Distinctions of Oxygen Uptake During Physical Exercise After Long-Term Restriction of Man's Motor Activity," candidatorial dissertation, Moscow, 1966.

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CONNECTIVE TISSUE OF SKELETAL MUSCLES AND THE MYOCARDIUM UNDER HYPOKINETIC CONDITIONS AND COMBINATION THEREOF WITH PHYSICAL LOADS

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[Article by P. P. Potapov, submitted 13 Jun 78]

Morphological studies under hypokinetic conditions revealed dystrophic changes in skeletal muscles and the myocardium, which were associated with development of connective tissue [1-4]. The quantitative biochemical characteristics of sclerotic changes in muscles were described previously [5]. In this work, we studied the effectiveness of regular exercise [physical loads] as a factor preventing development of these disturbances.

Methods

The study was conducted on 159 albino rats (49 of which served as a control) weighing 180-220 g. The first group of experimental animals (hypokinesia) were put in small individual cages made of plexiglas; the second group of rats was submitted to a physical load, consisting of swimming every third day in water with temperature of 31-32°C. Swimming time was gradually increased from 5 min at the beginning of the experiment to 40 min on the 16th day. Thereafter, the swimming time was constant to the end of the experiment, constituting 40 min [6]. The third group of animals (hypokinesia combined with exercise) was kept in small cages and they were exercised on the same schedule. Control rats were kept in the usual vivarium cages. All of the animals were in the same room and fed a completre diet with water ad lib. The rats were decapitated on the 15th, 30th, 60th and 90th experimental days. Control animals were sacrificed and examined concurrently with experimental ones. We examined the ventricular myocardium and tissue of skeletal muscles (without tendons or fascia) from the posterior group of femoral muscles. Wet tissue was ground in a mortar and treated successively with acetone and an ether-acetone mixture (3:1) for 1 h at 40°C, as recommended by Mier and Wood [7]. We assayed hydroxyproline [8], hexosamines [9] and hexuronic acids [10] in hydrolysates of dry tissue acetone powder. Determination of these parameters enables us to judge the amount of collagen, total aminopolysaccharides and glucosamine glycuronans (acid glucosamine glycans) in tissues.

Results and Discussion

Restriction of movement led to a significant increase in hydroxyproline content of skeletal muscles. The greatest changes were demonstrated on the 90th day, when the increment constituted 48.3% ($P<0.01$), as compared to the control (Table 1). There was also an increase in amount of this amino acid in cardiac tissue, by 4.2 and 7.6% ($P<0.05$) on the 60th and 90th days, respectively.

Table 1. Hydroxyproline content of rat tissues as related to different regimens of motor activity (mg/100 g dry defatted tissue), M±m

Tissue	Factor	Control	Day of experiment			
			15th	30th	60th	90th
Skeletal muscles	Hypokinesia	226,1 ± 5,0 (25)	315,7 ± 8,5** (9)	309,0 ± 9,7** (8)	334,8 ± 8,7** (8)	335,4 ± 7,7** (8)
	Exercise	292,9 ± 3,4 (22)	292,8 ± 8,0 (8)	291,6 ± 8,1 (8)	291,0 ± 8,1 (8)	290,4 ± 10,2 (8)
	Hypokinesia + exercise	292,9 ± 3,4 (22)	381,6 ± 21,6** (8)	396,4 ± 13,7** (8)	398,4 ± 12,8** (8)	390,2 ± 14,3** (10)
Heart	Hypokinesia	360,6 ± 3,2 (20)	359,5 ± 5,1 (9)	360,7 ± 5,9 (8)	376,0 ± 5,4** (8)	388,0 ± 6,1** (8)
	Exercise	385,6 ± 7,0 (19)	376,5 ± 9,4 (8)	396,5 ± 11,9 (8)	402,0 ± 17,3 (8)	359,3 ± 8,0** (8)
	Hypokinesia + exercise	385,6 ± 7,0 (19)	386,3 ± 11,9 (8)	425,3 ± 14,0** (8)	416,3 ± 16,3* (8)	399,8 ± 17,3 (8)

Note: Here and in Table 2, the number of animals is given in parentheses.
*$0.05<P<0.1$ **$P<0.05$

Hexosamine content dropped on the 30th day in the myocardium and on the 15th, 30th and 90th days of hypokinesia in skeletal muscles. At the end of the 2d month of the experiment, there was elevation of hexosamine level in skeletal muscles and myocardium by 12.6 and 8.9% ($P<0.05$), respectively.

Under hypokinetic conditions, there was negligible decrease in hexuronic acid content of the heart, while it increased by 12.3, 5.1 and 7.8% ($P<0.05$) on the 30th, 60th and 90th days, respectively, in skeletal muscles (Table 2).

The exercise did not elicit appreciable changes in these parameters in healthy rats, with the exception of a decrease by 6.8% ($P<0.05$) in hydroxyproline content of the heart on the 90th experimental day.

Table 2. Hexosamine and hexuronic acid content in rat tissues as related to different regimens of motor activity (mg/100 g dry defatted tissue), M±m

Tissue	Factor	Control	Day of experiment			
			15th	30th	60th	90th
	Hexosamines					
Skeletal muscle	Hypokinesia	236.0±5.4 (25)	215.7±5.3** (9)	213.8±4.7** (9)	257.0±9.0** (8)	189.8±10.4** (8)
	Exercise	255.3±4.4 (22)	257.3±6.9 (8)	245.8±9.5 (8)	256.5±6.8 (8)	248.0±5.7 (9)
	Hypokinesia + exercise	255.3±4.4 (22)	258.8±9.8 (8)	260.3±8.1 (8)	275.3±9.8* (8)	278.3±11.5* (9)
Heart	Hypokinesia	384.2±10.4 (18)	380.8±8.4 (9)	349.7±9.1** (8)	432.9±17.4** (8)	407.5±16.1 (8)
	Exercise	423.8±15.7 (22)	415.3±16.3 (8)	411.3±14.0 (8)	441.8±24.7 (8)	414.4±25.3 (9)
	Hypokinesia + exercise	423.8±15.7 (22)	430.3±25.3 (8)	387.2±24.3 (8)	397.5±21.1 (9)	413.3±14.2 (9)
	Hexuronic acids					
Skeletal muscle	Hypokinesia	63.2±0.7 (25)	60.7±1.8 (9)	71.0±1.9** (8)	66.4±1.2** (8)	68.1±1.5** (8)
	Exercise	64.0±0.7 (24)	63.6±1.6 (8)	63.0±1.5 (8)	64.4±0.7 (8)	63.6±1.0 (8)
	Hypokinesia + exercise	64.0±0.7 (24)	66.3±1.3 (9)	69.4±1.8** (8)	70.9±2.2** (8)	71.6±1.7** (10)
Heart	Hypokinesia	157.9±4.4 (20)	166.0±7.8 (9)	149.8±6.3 (8)	137.3±11.1* (8)	144.0±16.6 (8)
	Exercise	164.2±9.3 (24)	164.0±8.3 (8)	167.5±13.1 (9)	144.8±16.7 (8)	157.3±10.1 (9)
	Hypokinesia + exercise	164.2±9.3 (24)	162.3±16.4 (9)	150.3±15.7 (8)	166.3±10.3 (9)	143.5±7.3 (8)

There was less increase in hydroxyproline content of skeletal muscle tissue in rats submitted to the combination of hypokinesia and physical loads than in the first group of rats; however, even so the increment constituted 35-36% ($P<0.01$), as compared to the control. Hexuronic acid level in skeletal muscles was increased by 8.4, 10.8 and 11.9% in animals of the third group, on the 30th, 60th and 90th days ($P<0.05$), respectively; at the late stages, we observed a tendency toward increase in hexosamine content of this tissue. In these rats, hexosamine and hexuronic acid content of the myocardium showed virtually no change throughout the 3-month experimental period, while hydroxyproline increased by 10.3% ($P<0.05$) on the 30th day.

During development of connective tissue, the increase in concentration of acid glucosamine glycans plays the role of an inductor in formation of collagen structures [11, 12]. Under hypokinetic conditions, hydroxyproline content increased as early as the 15th day in skeletal muscles, while accumulation of glucosamine glycuronans was demonstrated only 1 month after the start of the experiment. In heart tissue, collagen content increased against a background of somewhat lower level of hexuronic acids. All this warrants the assumption that, in this instance, accumulation of collagen was not related to more intensive synthesis thereof, but to more intensive dissociation of muscular proteins proper, which implement contractile function. This hypothesis is also confirmed by data pertaining to the general tendency toward depressed protein synthesis under hypokinetic conditions [13].

On the 60th and 90th days of restricted mobility, the hydroxyproline/hexuronic acid ratio (according to molar concentration) increased by 42 and 38% in skeletal muscles, and by 20 and 18% in the myocardium. These disturbances indicate that there is a significant shortage of the main substance of intramuscular connective tissue under hypokinetic conditions. It is interesting to note that such changes in proportion of fibrous elements and main substance are observed during development of age-related changes in connective tissue [14, 15]. In the opinion of some authors, such changes in connective tissue structures are an important factor in aging of the entire organism [16].

In animals submitted to the combined effect of both factors, the increase in hexuronic acid content of skeletal muscles was more significant at the late stages of the experiment than in the first group of rats. Regular exercise apparently caused some normalization of carbohydrate metabolism in animals kept under hypokinetic conditions [17], and this in turn prevented onset of significant changes in normal proportion of fibrous elements and main substance of connective tissue.

In the third group of rats, the increase in hydroxyproline content of heart tissue was observed earlier, and it was even somewhat more marked than with "pure" hypokinesia. There is a decline of functional reserve of the myocardium when mobility is restricted [18]. Perhaps, under such conditions,

the additional load of swimming exceeded the adaptation capabilities of the myocardium, as a result of which there was a tendency toward development of cardiodystrophy. Thereafter, collagen content of the heart dropped to normal levels. It must be borne in mind that intensification of physical loads could lead to more severe and irreversible changes.

Thus, physical loads of the chosen intensity and duration did not prevent sclerotic changes in skeletal muscles under hypokinetic conditions. In order to improve the efficacy of exercise, it should be graduated on a strictly individual basis and used in conjunction with other preventive methods.

BIBLIOGRAPHY

1. Bykov, G. P., and Smirnov, V. P. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1970, pp 46-51.

2. Portugalov, V. V.; Il'ina-Kakuyeva, Ye. I.; and Starostin, V. I. Ibid, No 3, 1972, pp 15-17.

3. Vikhert, A. M.; Metelitsa, V. I.; Baranova, V. D.; et al. KARDIOLOGIYA [Cardiology], No 9, 1972, pp 143-146.

4. Bevzyuk, V. S. "Morphology of the Intraparietal Vascular System of the Heart Under Hypodynamic Conditions," author abstract of candidatorial dissertation, Dushanbe, 1975.

5. Potapov, P. P. KOSMICHESKAYA BIOL., No 3, 1977, pp 44-48.

6. Pinchuk, V. M.; Levina, L. I.; and Popov, V. N. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 5, 1973, pp 18-20.

7. Mier, P. D., and Wood, M. CLIN. CHIM. ACTA, Vol 24, 1969, pp 105-110.

8. Zaydes, A. L.; Mikhaylov, A. N.; and Pushenko, O. I. BIOKHIMIYA [Biochemistry], No 1, 1964, pp 5-7.

9. Gatt, R., and Berman, E. R. ANALYT. BIOCHEM., Vol 15, 1966, pp 167-171.

10. Dische, Z. J. BIOL. CHEM., Vol 167, 1947, pp 189-198.

11. Klimovich, L. G. "Study of Muscular Glucosamine Glycans After Denervation and Subsequent Stimulation," author abstract of candidatorial dissertation, Dnepropetrovsk, 1974.

12. Mathews, M. B., and Decker, L. BIOCHEM. J., Vol 109, 1968, pp 517-526.

13. Fedorov, I. V.; Chernyy, A. V.; and Fedorov, A. I. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 8, 1977, pp 1128-1133.

14. Clausen, B. LAB. INVEST., Vol 11, 1962, pp 229-234.

15. Idem, Ibid, pp 1340-1345.

16. Nikitin, V. N., et al. (editors) "Chief Ontogenetic Factors," Kiev, 1972, pp 6-43.

17. Chernyy, A. V. "Effect of Hypodynamia on Animals' Reactions to Administration of Glucose, Adrenalin, Insulin, and Some of the Parameters of Carbohydrate Metabolism," author abstract of candidatorial dissertation, Yaroslavl', 1974.

18. Pruss, G. M., and Kuznetsov, V. I. KOSMICHESKAYA BIOL., No 6, 1974, pp 45-49.
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